FATIGUE DURING MULTIJOINT EXERCISE: BIOMECHANICAL CENTRAL, PERIPHERAL, AND AGE-RELATED ASPECTS

by

Steven Joseph Elmer

A dissertation submitted to the faculty of
The University of Utah
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

Department of Exercise and Sport Science

The University of Utah

December 2011

The University of Utah Graduate School

STATEMENT OF DISSERTATION APPROVAL

The dissertation of **Steven Joseph Elmer**

has been approved by the following supervisory committee members:

James C. Martin	, Chair	**10-28-11** Date Approved
Markus Amann	, Member	**10-28-11** Date Approved
J. David Symons	, Member	**10-28-11** Date Approved
John McDaniel	, Member	**10-28-11** Date Approved
David T. Martin	, Member	**10-28-11** Date Approved

and by **Barry B. Shultz** , Chair of

the Department of **Exercise and Sport Science**

and by Charles A. Wight, Dean of The Graduate School.

ABSTRACT

Exercise-induced fatigue is often evaluated during isometric tasks that involve a small muscle mass. The purpose of this dissertation was to utilize dynamic exercise including a large muscle mass to provide additional insight into biomechanical, central, peripheral, and age-related aspects of fatigue. Specifically, I used high-intensity submaximal cycling (SUB_{cyc} time trial) to induce fatigue and quantify associated effects via pre- to postexercise changes in maximum cycling (MAX_{cyc}) power including joint-specific powers and power-rpm relationships. In the first study, I evaluated the effects of fatigue on changes in SUB_{cyc} and MAX_{cyc} joint-specific powers. Joint-specific powers were maintained during SUB_{cyc} but were substantially compromised during subsequent MAX_{cyc}. Changes in MAX_{cyc} power manifested with differential power loss at each joint with ankle plantar flexion (-43%) and knee flexion (-52%) exhibiting relatively greater fatigue than knee extension (-124%) and hip extension (-28 ± 6%). These data demonstrate that exercise-induced fatigue can have distinct consequences for MAX_{cyc} but not for SUB_{cyc} joint-specific power production. For the second study, I induced fatigue in one leg and examined whether fatigue "crossed-over" to the rested contralateral leg. Despite considerable power loss in the fatigued leg (-22%), MAX_{cyc} power was maintained in the rested leg. Thus, a cross-over of fatigue was either not present or not large enough to impair MAXcyc power in the rested leg. These results along with the lack of changes in maximum isometric handgrip force indicate that impairments in

voluntary neuromuscular function were specific to those muscles involved in the fatiguing task. In my third study, I evaluated the effects of aging on the development of functional consequences of fatigue. Even with > 30 yr difference in age (26 ± 4 vs. 57 ± 5 yr), masters cyclists exhibited nearly identical levels of fatigue compared to young in the fatigued leg (-21 vs. -22%). Similar to young, masters cyclists were able to overcome fatigue in this leg and produce the same baseline MAX_{cyc} with the rested leg. These results likely represent a best case scenario for healthy active aging. Collectively, these results provide insight into changes in dynamic neuromuscular function associated with high-intensity endurance exercise.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGMENTS

I would like to sincerely thank committee members James Martin, Markus Amann, John McDaniel, David Martin, and J. David Symons for their guidance during this project. In addition, I would like to acknowledge the following individuals who assisted with data collection: Jackie Bohn, Christopher Call, Skye Marshall, and Kyle Wehmanen. Finally, I would like to thank the participants for their enthusiastic efforts during the cycling trials.

1. INTRODUCTION

Fatigue is a complex process that has intrigued scientists for well over a century. Specifically, exercise-induced fatigue can be defined as a reversible reduction in the force- and power-generating capacity of the neuromuscular system (19). Fatigue also encompasses sensations that relate to tasks being more difficult or requiring more effort than expected (84). In healthy individuals, fatigue can impair performance during occupational related tasks (e.g., firefighting, laboring) and also limit participation in recreational activities and sports (63). Further, in diseased patients, fatigue can restrict activities of daily living and impair quality of life (63). Because of the wide range of activities that can elicit fatigue it is imperative to understand the functional outcomes associated with this process. Such an understanding would be useful for clinical, basic, and applied scientists and have implications for improving exercise prescription and training.

Traditionally, investigators have used isometric tasks involving small muscle mass to induce fatigue and evaluate recovery of neuromuscular function. For example, Gandevia and colleagues (46) induced fatigue via 3 min of sustained isometric elbow flexion and reported that maximum isometric force was reduced by 74%. Single-joint isometric protocols facilitate excellent measurement of neuromuscular function before, during, and after fatiguing exercise. They also allow for evaluation of central (45) and peripheral (4) components of fatigue. Most locomotor tasks, however, are performed

with multijoint, multi-degree of freedom actions that involve the large muscle mass of the legs (e.g., walking, climbing stairs). Using a *dynamic large muscle mass model* to induce fatigue and quantify changes in neuromuscular function may offer additional insight into the functional outcomes associated with fatigue and extend upon previous small muscle mass models.

Over the past decade, there has been growing interest in the notion that older individuals may be more fatigue-resistant compared to young individuals. Recently, Christie and colleagues (28) performed a systematic review and meta analysis of muscle fatigue and aging and concluded that older individuals do in fact develop less fatigue than younger individuals during isometric muscle contractions. Their results also indicated that older individuals develop greater fatigue during dynamic muscle contractions. These authors emphasized the need for additional studies to evaluate age-related differences in fatigue particularly during *dynamic exercise* as muscular power is important for maintaining physical function and independence with advanced age (14, 44).

For this dissertation, I used a dynamic large muscle mass model to investigate biomechanical, central, peripheral, and age-related aspects of fatigue during dynamic multijoint exercise. Specifically, I used high-intensity cycling (i.e., time trial) to induce fatigue and quantified fatigue via pre- to post exercise changes in maximum cycling power. In the first study I investigated the effects of fatigue on submaximal and maximal joint-specific power production. In the subsequent investigation, I examined the effects of voluntary muscle fatigue in one leg and determined whether fatigue "crossed-over" to the rested contralateral leg. In the third investigation, I evaluated the effects of aging on the development of fatigue. Collectively, the anticipated results from these studies may

have implications for researchers, clinicians, as well as coaches and athletes. In the subsequent sections of this dissertation (Sections 2, 3, 4) I discuss each of these studies in detail and provide an overall summary, conclusion, and recommendations for future research in the final chapter (Sections 5).

2. INFLUENCE OF EXERCISE-INDUCED FATIGUE ON SUBMAXIMAL AND MAXIMAL JOINT-SPECIFIC POWER PRODUCTION

Many activities, including training for endurance and power sports, work-related manual labor, and activities of daily living can induce fatigue. Fatigue can be defined as a reversible reduction in the force- and power-generating ability of the neuromuscular system (19, 43). Several previous authors (16, 26, 56, 77, 89) have used high-intensity submaximal cycling (e.g., 80% of peak power reached during VO_{2max}) to induce fatigue and subsequently quantified fatigue via pre- to postexercise changes in maximum cycling power. In these studies maximum cycling power was reduced up to 32% following high-intensity submaximal cycling. The effect of fatigue on cycling power is interesting, but equally important is the effect of fatigue on the power produced by ankle, knee, and hip joint actions (23, 38, 40, 86). Thus, reductions in cycling power (measured at the pedals) following high-intensity cycling represents the net decrease for joint-specific power loss but does not indicate which joint actions (e.g., knee extension) were impaired. Depending on the strategies used to produce power during high-intensity submaximal cycling, subsequent maximal joint-specific power production could be equally reduced across the ankle, knee, and hip or may be more reduced predominately at one specific joint (59). For example, a decrease in knee extension power during high-intensity cycling might predict pre- to postexercise changes in that joint action power. However, measurements of joint-specific power production *during* high-intensity submaximal

cycling along with *pre- to postexercise* changes in maximal cycling joint-specific powers have not been reported.

Recently, several authors (3, 25, 54, 57, 58) have debated possible mechanisms responsible for task failure during high-intensity endurance exercise. Marcora and Staiano (56) reported that maximum cycling power measured immediately after task failure during with high-intensity constant power cycling was over three times as high as the power that elicited task failure (242 vs. 731 W). These authors concluded that task failure was regulated primarily by rating of perceived exertion (RPE) rather than neuromuscular fatigue because participants had considerable reserve upon reaching task failure. Subsequently, several authors (3, 25, 54) have challenged this conclusion as some of the observed differences in power could have primarily resulted from differences in pedaling rate between submaximal and maximal cycling (i.e., power-velocity relationships). Using a similar pedaling rate (e.g., 90 rpm) for each cycling condition could eliminate differences due to pedaling rate and provide further insight into the mechanisms associated with sensory tolerance during high-intensity endurance exercise.

Understanding the influence of exercise-induced fatigue on submaximal and maximal joint-specific power production may be useful for researchers as well coaches and athletes. Specifically, researchers who use cycling as a fatigue model may need to know whether pre- to postexercise changes in knee extensor function (e.g., maximum voluntary isometric force) are similar to those changes in other muscle groups involved with the cycling task (e.g., hip extensors). In addition to laboratory-based cycling protocols, competitive cycling is inherently a non-steady state activity (71) and insight

into how joint-specific powers change with fatigue may have practical applications for coaches and athletes when evaluating performance and implementing training programs.

The purpose of this study was to evaluate joint-specific power production *during* high-intensity submaximal cycling and compare *pre- to postexercise* changes in maximal cycling joint-specific powers. We recently reported that hip extension is the dominate power producing action during submaximal and maximal cycling (38). Therefore, we hypothesized that hip extension would produce the most power during high-intensity submaximal cycling and that this joint action would exhibit the greatest reduction in power during subsequent maximal cycling.

Methods

Participants

Ten male cyclists (age: 30 ± 7 yrs; mass: 74 ± 13 kg; height: 1.76 ± 0.06 m) volunteered to participate in this study. Experimental procedures used in this investigation were reviewed by the University of Utah Institutional Review Board and all participants provided written informed consent prior to testing. Participants reported to the laboratory prior to the experimental day in order to become familiar with the isokinetic ergometer and maximal cycling trials (described below). Briefly, the ergometer seat height was adjusted to match each participant's accustomed cycling position and participants wore cycling shoes that interfaced with Speedplay pedals (Speedplay Inc., San Diego, CA, USA). Participants cycled for 5 min at a self-selected intensity (90 rpm) and then performed four maximal 3 s cycling trials (90 rpm) with 2 min of rest in between trials.

Experimental protocol

On the experimental day participants reported to the laboratory where body mass, height, thigh length (greater trochanter to lateral femoral condyle), shank length (lateral femoral condyle to lateral malleolus), foot length (heel to toe), and kinematic foot length (pedal spindle to lateral malleolus) were recorded. Following a 5 min cycling warm-up (75-150 W at 90 rpm) participants performed a maximal cycling trial (3 s) on an isokinetic ergometer at 90 rpm. After 2 min of recovery, participants performed a self-paced maximal effort time trial (TT, 10 min) on an isokinetic ergometer at 90 rpm. Participants were instructed to cycle as "hard as you can go" for the 10 min period and were provided with strong verbal encouragement throughout the TT. Mean cycling power was quantified using a power meter (Schoberer Rad Messtechnik, SRM, Jülich, Germany), a system that has previously been shown to accurately quantify power output (2, 47, 60). During the final 30 s of the TT overall rating of perceived exertion ($RPE_{overall}$), leg perceived exertion (RPE_{legs}), and heart rate (Polar CS300, Kempele, Finland) were assessed. Within 15 s of the end of the TT, participants again performed a maximal cycling trial (3 s). Whole blood lactate (ARKRAY Lactate Pro LT-1710, Kyoto, Japan) was measured 1 min after the TT. Note that participants were instructed to remain seated throughout each cycling protocol. Exercised-induced fatigue was quantified as the pre- to post-TT change in maximal cycling power and joint-specific powers.

Isokinetic ergometer

A Monark (Vansbro, Sweden) cycle ergometer frame and flywheel was used to construct the isokinetic ergometer (38, 59). The flywheel was driven by a 3.8 kW direct current motor (Baldor Electric Company model CDP3605, Fort Smith, AR, USA) via

pulleys and a belt. The motor was controlled with a speed controller (Minarik RG550U, Glendale, CA, USA) augmented with feedback (Minarik DLC600) and a mechanical brake. Addition of the mechanical brake (standard Monark ergometer pendulum augmented with additional mass) forced the motor to function in driving mode rather than braking mode throughout the cycling trial. The right pedal was equipped with two 3-component piezoelectric force transducers (Kistler 9251: Kistler USA, Amherst, NY, USA), and the right pedal and crank were equipped with digital position encoders (U.S. Digital model S5S-1024: Vancouver, Washington, USA).

Kinematic and kinetic data

Two-dimensional kinematic and kinetic cycling data were obtained using the methods described in recent papers from our laboratory (38, 59). Briefly, pedal forces, pedal and crank positions, and the position of an instrumented spatial linkage system (ISL) were recorded at 240 Hz. Normal and tangential pedal forces, pedal position, crank position, and ISL position data were filtered using a fourth-order zero-lag low-pass Butterworth filter with a cutoff frequency of 8 Hz. Pedal power was calculated as the dot product of pedal force and linear pedal velocity. Positions of the right greater trochanter and iliac crest were determined at rest with the ISL and the relative position were assumed to remain constant (67). During the cycling trials iliac crest and pedal and crank position coordinates were recorded, which allowed sagittal plane limb segment positions to be determined geometrically. Linear and angular velocities and accelerations of the limb segments were determined by finite differentiation of position data. Segmental masses, moments of inertia, and location of centers of mass were estimated using the regression equations reported by de Leva (33). Sagittal plane joint reaction forces and

net joint moments at the ankle, knee, and hip were determined using inverse dynamics (37). Ankle, knee, and hip joint-specific powers were calculated as the product of net joint moments and joint angular velocities. Power transferred across the hip joint was calculated as the dot product of the hip joint reaction force and linear velocity.

For maximal cycling trials, joint-specific powers were analyzed for 3 s. During the TT joint-specific powers were analyzed for 30 s intervals: 1) early-TT: 30-60 s, 2) middle-TT: 270-300 s, and 3) late-TT: 570-600 s. Joint-specific powers were averaged over all of the complete pedal cycles within each measurement interval. Additionally, joint-specific powers were averaged over the extension and flexion phases, which were defined by joint-angular velocity directions (59). Note that because most power is produced during the extension phase, power values averaged over the extension phase can be larger than those averaged over complete pedal cycles. Finally, joint-specific power data from previous investigations (23, 38, 40, 59, 86) generally have indicated that ankle plantar flexion, knee extension, knee flexion, and hip extension are the four main power producing actions during submaximal and maximal cycling, and thus we were most interested in understanding fatigue associated with these joint actions.

Data analysis

Time trial (TT) variables (power, heart rate, lactate, $RPE_{overall}$, RPE_{legs}) are reported for descriptive purposes. A two-way repeated measures analysis of variance (ANOVA) was used to evaluate changes in joint-specific powers produced during the TT (early-TT, middle-TT, late-TT). Pre- to post-TT changes in maximal cycling joint-specific powers were also assessed with a two-way repeated measures ANOVA. Magnitudes of relative pre- to-post changes in maximal cycling joint-specific powers

(i.e., joint-specific fatigue indices) were assessed with a one-way ANOVA. Differences in joint-specific powers produced during the final 3 s of the TT and post-TT maximal cycling trial were compared using a two-way repeated measures ANOVA. If any of the ANOVA's indicated significant main effects then subsequent post hoc analyses (Fisher least significant difference test) were performed to identify where differences occurred. Data were presented as mean ± standard error of the mean (SEM) and alpha was set to 0.05.

Results

Mean power produced during the 10 min TT was 288 ± 10 W. Heart rate, $RPE_{overall}$, and RPE_{legs} assessed during the final 30 s of the TT were 184 ± 3 b min^{-1}, 19.0 ± 0.2 scale units, and 19.0 ± 0.3 scale units, respectively. Whole blood lactate measured after the TT was 12.8 ± 0.6 mmol L^{-1}. During the TT hip extension power was greater than all other joint-specific powers ($P < 0.001$, Table 1, Figure 2.1). Knee extension power was greater than all other joint powers except hip extension ($P < 0.001$, Table 2.1; Figure 2.1). Ankle plantar flexion and knee flexion powers were similar during the TT ($P = 0.75$). Pedal and joint-specific powers did not differ during the early, middle, and late stages of the TT ($P = 0.16$).

Compared with pre-TT, pedal power produced during maximal cycling was reduced by 32 ± 3% ($P < 0.001$, Table 2.2 and Figure 2.2) post-TT. Post-TT ankle plantar flexion power was reduced by 43 ± 5% ($P < 0.001$, Table 2.2, Figure 2.2). Post-TT knee extension and knee flexion powers were reduced by 12 ± 4% and 52 ± 5%, respectively, ($P < 0.05$, $P < 0.001$, respectively, Table 2.2, Figure 2.2). Post-TT hip extension, was reduced by 28 ± 6% post-TT ($P < 0.01$, Table 2.2, Figure 2.2).

Magnitudes of relative pre- to post-TT changes in ankle plantar flexion (43 ± 5%) and knee flexion powers (52 ± 5%) were not different but were greater than those changes in relative knee extension (12 ± 4%) and hip extension powers (28 ± 6%) ($P < 0.05$, Table 2.2, Figure 2.2). Relative changes in knee extension power (12 ± 4%) and hip extension powers (28 ± 6%) did not differ but were approaching significance ($P = 0.09$, Table 2.2, Figure 2.2). Post-TT maximal cycling pedal and joint-specific powers were greater than those powers produced during the final 3 s of the TT ($P < 0.05$, Figure 2.3).

Discussion

In this investigation, we used high-intensity submaximal cycling (i.e., self paced 10 min TT) to induce fatigue and subsequently quantified fatigue via pre- to post-TT changes in maximal cycling joint-specific powers. Participants were trained cyclists and highly motivated to give their best and therefore most fatiguing effort within the TT. Our results indicated that joint-specific powers were maintained during the TT but were substantially compromised during subsequent maximal cycling. That is, participants produced TT power with similar joint-specific contributions throughout the trial. Conversely, joint-specific power production during subsequent maximal cycling manifested with differential, rather than equal, power loss at each joint. Specifically, ankle plantar flexion and knee flexion exhibited relatively greater fatigue than knee extension and hip extension. Despite working near maximal effort at the end of the TT, participants were still able to produce much higher power immediately after the TT, suggesting that they had considerable neuromuscular reserve. Taken together, these results demonstrate that exercise-induced fatigue can have distinct functional effects on submaximal and maximal joint-specific power production strategies.

Time trial joint-specific powers

During the TT, cyclists tended to employ the characteristic "U" shaped pacing pattern (higher, lower, higher power) which is consistent with previous reports (7, 8). However, small fluctuations in pedal power were not associated with significant changes in joint-specific powers. Based on recent work from our laboratory (38) we would expect that only large changes in pedal powers would signify changes in joint-specific powers. Therefore, our findings of differential joint-specific fatigue during maximal cycling were not presaged by changes in submaximal joint-specific power production. That is, we did not observe a significant decrease in, for example, TT knee extension power that would predict pre- to post-TT changes in that joint action power. To the best of our knowledge, we are the first group to evaluate changes in joint-specific power characteristics during a TT. Previous authors (21, 75) have evaluated joint-specific changes during high-intensity constant power cycling but reported only measures of joint-specific torque, rather than power, which excludes the importance of velocity. Thus, these data extend on previous work and document power production at individual joints during high-intensity submaximal cycling.

Maximal cycling joint-specific powers

After the TT, pedal power was reduced by 32% which supports previous findings (16, 56, 77, 89) of 25-32% reductions in maximum cycling power and also indicates that the TT was effective in altering neuromuscular function. Reductions in pedal power were due to significant power loss at the ankle, knee, and hip and power transferred across the hip. However, relative ankle plantar flexion and knee flexion exhibited more fatigue than knee extension and hip extension. Thus, these results demonstrate that the self-paced

maximal effort 10 min TT induced differential, rather equal, fatigue at each joint. These data are in general agreement with work by Martin and Brown (59) who reported differential joint-specific fatigue during 30 s maximal cycling with ankle plantar flexion exhibiting the most fatigue. Although there is some agreement between our findings and those of Martin and Brown (59) there were also differences. Specifically, in the current study knee extension was relatively fatigue resistant whereas Martin and Brown (59) reported that knee extension was quite fatigable (12% vs. 59% decrease in knee extension power, respectively). Also, magnitudes of relative changes for other joint actions differed as well between the two studies. Such differences could be related to total work and power produced during the fatiguing trial, pedaling rate (90 vs. 120 rpm), disturbances in the metabolic milieu within the muscle, peripheral fatigue, and/or central fatigue (34, 42). These comparisons demonstrate that joint-specific fatigue is highly dependent on the duration and intensity of the exercise as well as the methods used to quantify fatigue.

Although hip extension exhibited moderate fatigue when expressed in relative power terms, it exhibited the greatest reduction in absolute power. In addition, hip extension was the dominate power producing action during the TT as well as during maximal cycling, which is consistent with recent work by Elmer and colleagues (38). Therefore, these absolute power data indicate that the joint action that produced the most power during the TT, exhibited the greatest reduction in absolute power during maximal cycling which supports our hypothesis. Based on these results it was not surprising that relative reductions in hip extension power were quite similar to those reductions in pedal

power (28% vs. 32%). Collectively, these results highlight the important role of hip extension actions during submaximal and maximal cycling.

Influence of motor control strategies

It is important to point out that joint-specific power loss and fatigue may have been influenced in part by changes in motor control strategies as cycling is a multijoint, multiple degree of freedom movement. For example, hamstring bi-articular muscles cross the knee and the hip and in a fatigued state there may have been a tradeoff to maximize hip extension power at the expense of reducing knee flexion power. Indeed, relative knee flexion power was reduced to a much greater extent than relative hip extension power (52% vs. 28%). In support of this explanation, data from Decorte and colleagues (34) indicate that maximum voluntary isometric force of knee flexors was in fact maintained following high-intensity submaximal cycling. Alterations in motor control strategies may have also contributed to the large reductions in relative ankle plantar flexion power. Ankle plantar flexion actions are primarily responsible for transferring power produced at the knee and hip across the ankle to the pedal. As suggested by Martin and Brown (59), reduced ankle plantar flexion power and range of motion with fatigue may represent a strategy to minimize power loss across the ankle joint to the pedal. Indeed, knee extension and hip extension exhibited relatively less fatigue compared to ankle plantar flexion.

Interestingly, relative reductions in knee extension power (12%) are similar to reductions in maximum voluntary isometric force of knee extensors (8-14%) (7, 8, 10, 34) following high-intensity submaximal cycling. This could suggest that reduced knee extension power in this investigation was mostly due to fatigue with changes in motor

control playing a lesser role. The extent to which changes in motor control contributed to the reductions in hip extension is unclear as pre- to postexercise changes in hip extensor function following high intensity submaximal cycling have not been reported. Within the scope of our present data, exact determination of the influence of motor control on joint-specific fatigue remains speculative. A next step would be to use forward dynamic simulations to quantify individual muscle forces and activation patterns (90) in order to elucidate the contributions of neuromuscular fatigue and motor control to multijoint fatigue.

Neuromuscular reserve capacity

Marcora and Staiano (56) recently reported that task failure during high-intensity constant power cycling was regulated by RPE rather than neuromuscular fatigue because participants had the ability to increase their power considerably after reaching task failure. Subsequently, this conclusion has been debated by several researchers (3, 25, 54) as some of the observed differences in power could have resulted from differences in pedaling rate between constant power and maximum cycling protocols. To address concerns raised by these authors, we designed this study so that pedaling rate (90 rpm) was the same for both the TT and maximal cycling trials. Although participants in the current study were working close to maximal effort (RPE of 19) at the end of the TT, they were also able to produce considerably greater power during post-TT maximal cycling (compared to final 3 s of the TT). As suggested by Amann (6), TT exercise intensity and power output are likely reduced once a critical rate of fatigue development and associated afferent feedback are reached. Consequently, power at the end of the TT may not represent the muscles' ultimate limit to produce power. Indeed, subsequent

short-term increases in power produced during post-TT maximal cycling provide evidence that the central nervous system is able to briefly override inhibitory feedback from muscle afferents even in conditions of substantial fatigue. Therefore, we interpret these results to indicate that participants had considerable neuromuscular reserve capacity for each joint action as well as the whole-leg action at the end of the TT. Further, sensory tolerance during high-intensity cycling is likely limited by central (17, 34, 79), peripheral (6-10, 12, 17, 34, 79), and/or psychological factors (56) with biomechanical factors playing a minor role. It is important to point out that power may have partially recovered within the short delay prior to the post-TT maximal cycling trial. However, the occurrence of such quick recovery is unlikely given that previous authors have reported that central (17, 34, 79) and peripheral fatigue (7-10, 12, 17, 34, 79) can last for several minutes.

Implications

Our findings relating to joint-specific power production and fatigue may have implications for researchers, clinicians, and athletes. Specifically, researchers who use cycling to induce fatigue, may consider evaluating pre- to postexercise changes in additional muscle groups to traditionally measured knee extensors. For example, changes in ankle plantar flexor function (e.g., potentiated twitch force, maximum voluntary isometric force) may differ from those changes in knee extensor function and provide additional insight into the mechanisms of joint-specific fatigue as well as the influence of motor control. Additionally, evaluation of changes in hip extensor function would be useful because hip extension is the dominate action during cycling (38) and thus heavily influences overall reductions in pedal power. In clinical settings, submaximal cycling

may serve as an appropriate exercise for targeting and rehabilitating hip extensors while also eliciting cardiovascular benefits. Finally, a practical application of our results is that competitive cyclists may benefit from training isolated muscle groups in order to possibly improve fatigue-resistance during cycling.

Summary

Joint-specific powers were maintained during high-intensity submaximal cycling but were compromised during subsequent maximal cycling. Specifically, ankle plantar flexion and knee flexion exhibited relatively greater fatigue than knee extension and hip extension indicating differential joint-specific fatigue. Although participants were working close to maximal effort at the end of the TT, they still had the ability to produce considerably more power after the TT. This suggests that participants had considerable neuromuscular reserve and that biomechanical factors did not likely limit sensory tolerance during the TT. These are the first data to document joint-specific power production *during* high-intensity submaximal cycling along with *pre- to postexercise* changes in maximal cycling joint-specific power characteristics and highlight the impact of exercise-induced fatigue on submaximal and maximal power production. These results may serve as bases for future research to elucidate the contributions of neuromuscular fatigue and motor control to multijoint fatigue.

Table 2.1: Submaximal joint-specific powers. Pedal and joint-specific powers produced during the early, middle, and late stages of the 10 min TT (90 rpm).

	Pedal and Joint-Specific Powers (W)				
	Pedal	**Ankle Plantar Flexion**	**Knee Extension[b]**	**Knee Flexion**	**Hip Extension[a]**
Early	144 ± 7	30 ± 4	68 ± 9	30 ± 6	149 ± 8
Middle	139 ± 6	25 ± 3	80 ± 9	27 ± 7	134 ± 12
Late	153 ± 7	25 ± 2	95 ± 12	30 ± 8	145 ± 16

Values are reported as mean ± SEM. Note that power was measured at the right pedal and thus pedal and joint-specific powers represent the power produced by one leg.

[a] Hip extension was the most powerful action

[b] Knee extension was more powerful than ankle plantar flexion and knee flexion

Table 2.2: Maximal joint-specific powers. Pre- to post-TT changes in pedal and joint-specific powers produced during maximal cycling (90 rpm).

	Pedal and Joint-Specific Powers (W)				
	Pedal	**Ankle Plantar Flexion**	**Knee Extension**	**Knee Flexion**	**Hip Extension**
Pre	492 ± 18	143 ± 10	227 ± 16	193 ± 12	363 ± 21
Post	331 ± 13[a]	82 ± 10[a,b]	202 ± 18[a]	91 ± 9[a,b]	254 ± 18[a]

Values are reported as mean ± SEM. Note that power was measured at the right pedal and thus pedal and joint-specific powers represent the power produced by one leg.

[a] Different than pre-TT value ($P < 0.05$)

[b] Ankle plantar flexion and knee flexion were relatively more fatigable than knee extension and hip extension

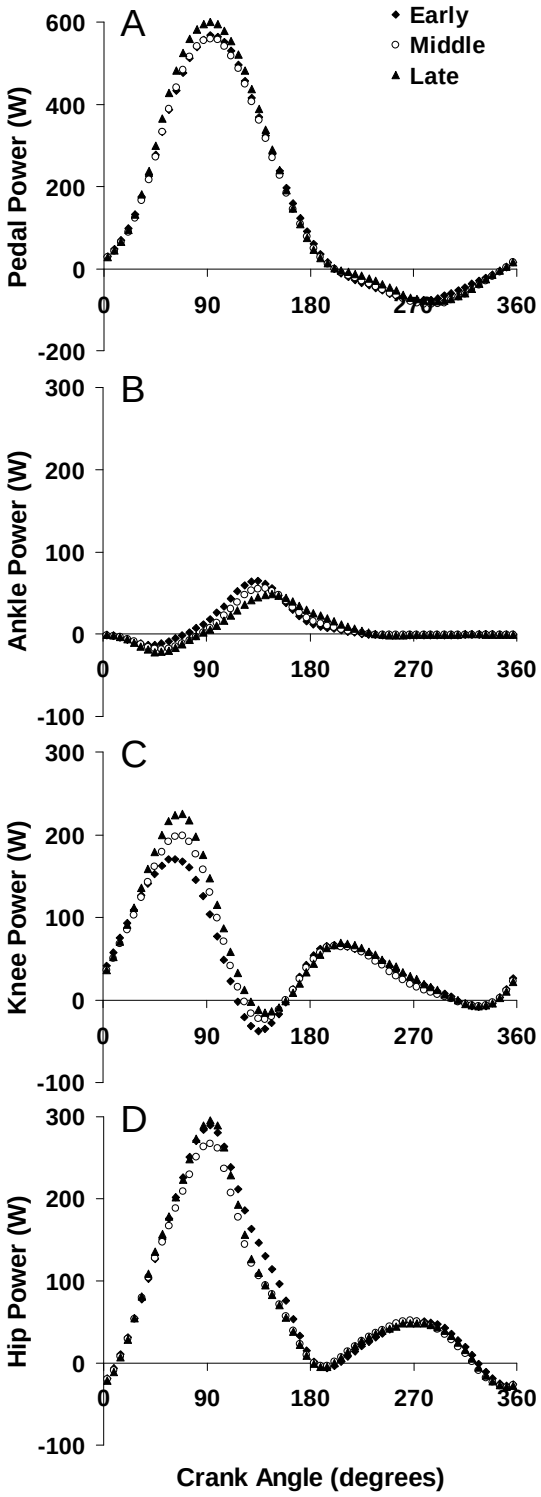

Figure 2.1: Time trial joint-specific powers. Instantaneous power (mean) produced at the pedal (A) and by ankle (B), knee (C), and hip (D) joint actions for all participants during the early, middle, and late stages of the TT (90 rpm). Crank angles of 0° and 360° represent the top dead center of the pedal position and 180° represents the bottom dead center of the pedal position. Note that power was measured at the right pedal and thus pedal and joint-specific powers represent the power produced by one leg. Standard error bars were removed for clarity.

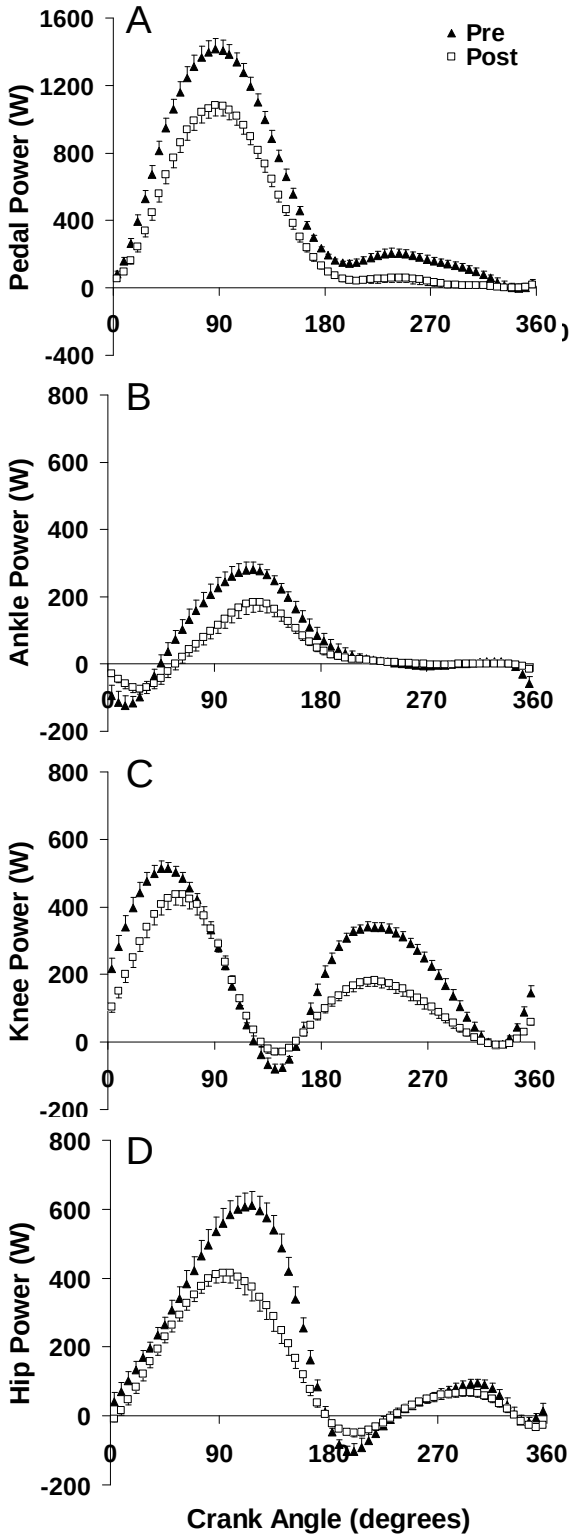

Figure 2.2: Maximal cycling joint-specific powers. Pre- to post-TT changes in maximal cycling joint-specific powers. Instantaneous power (Mean ± SEM) produced at the pedal (A) and by ankle (B), knee (C), and hip (D) joint actions for all participants during pre-TT and post-TT maximal cycling (90 rpm). Crank angles of 0° and 360° represent the top dead center of the pedal position and 180° represents the bottom dead center of the pedal position. Note that power was measured at the right pedal and thus pedal and joint-specific powers represent the power produced by one leg.

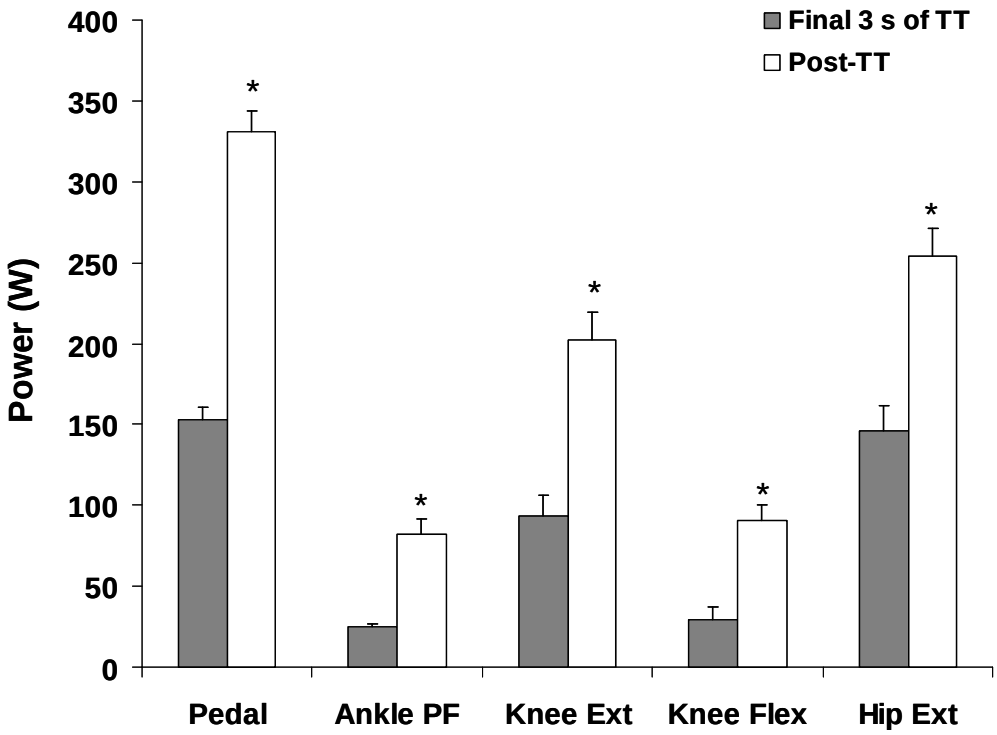

Figure 2.3: Estimate of neuromuscular reserve. Power (mean ± SEM) produced at the pedal (A) and by ankle (B), knee (C), and hip (D) joint actions for all participants during the final 3 s of the TT and post-TT maximal cycling (90 rpm). Note that power was measured at the right pedal and thus pedal and joint-specific powers represent the power produced by one leg. * different than final 3 s of the TT ($P < 0.05$).

3. FATIGUE IN ONE LIMB DOES NOT IMPAIR MAXIMAL VOLUNTARY NEUROMUSCUALR FUNCTION IN THE RESTED CONTRALATERAL LEG FOLLOWING HIGH-INTENSITY SINGLE-LEG CYCLING

Exercise-induced fatigue is defined as a reversible reduction in the force- and power-generating ability of the neuromuscular system (19, 43) and can manifest through central and/or peripheral mechanisms. Specifically, central fatigue results in a failure of the central nervous system to excite and drive motor neurons (45) whereas peripheral fatigue results in a failure of the muscle to respond to neural excitation (4). The development of central fatigue, as estimated via changes in voluntary muscle activation, is usually evaluated during a maximal isometric contraction of the exercising muscle. Similarly, exercise-induced peripheral muscle fatigue is usually quantified via the reduction in force output in response to direct electric / magnetic motor nerve stimulation shortly after, or during, muscle contractions. Central and peripheral fatigue are usually assessed in the exercised muscle.

Some previous authors (62, 72, 85), however, have induced fatigue in a single limb muscle and reported reductions in voluntary muscle activation in the rested contralateral homologous muscle. For example, Martin and colleagues (62) reported that sustained maximal isometric knee extension exercise in one leg reduced voluntary muscle activation of rested contralateral knee extensors by 9%. Because direct electrical stimulation of the contralateral knee-extensors revealed no peripheral muscle fatigue,

these results suggest a "cross-over" of central fatigue from a fatigued limb muscle to the rested contralateral homologous muscle. Although this *fairly small* cross-over of central fatigue was associated with a significant reduction in maximum voluntary isometric force of the rested contralateral muscle (62), not all investigations confirm this functional consequence (72, 85). This discrepancy could be explained by the fact that a small cross-over of central fatigue and the associated *small* reduction in voluntary muscle activation might not be sufficient to measurably impair the functional capacity of the rested contralateral muscle when fatigue is induced via a maximal isometric contraction of a single muscle. Furthermore, it is unknown if a cross-over of fatigue (central and/or peripheral in origin) also occurs when induced via high-intensity endurance exercise involving a substantial muscle mass. In addition, it is unclear whether a potential cross-over of fatigue would then have a more pronounced functional consequence for the previously rested contralateral muscles / muscle groups as compared to those observed following maximal isometric contraction of only a single muscle.

During locomotor exercise, potential cross-over effects of fatigue could be delineated by using a single-leg cycling model. That is, high-intensity single-leg cycling could be used to induce specific central and peripheral fatigue in the working leg. Subsequent evaluation of maximum cycling power in the rested contralateral leg and fatigued ipsilateral leg would offer a paradigm for examining the functional impact of exercised-induced fatigue as well as cross-over effects of fatigue. For example, if maximum power was reduced in the rested contralateral leg, this would indicate a cross-over effect of fatigue. Conversely, if maximum power was maintained in the rested

contralateral leg, this would indicate that fatigue was specific to those exercised muscles of the fatigued ipsilateral leg.

Therefore, the purpose of this study was to examine the effects of voluntary muscle fatigue in one leg on maximum power and determine whether fatigue crossed-over to the rested contralateral leg. Specifically, we induced fatigue via high intensity single-leg cycling and evaluated associated effects on maximum cycling power in the rested contralateral leg as well as the fatigued ipsilateral leg. We hypothesized that exercise-induced fatigue would result in a cross-over effect, impairing maximum cycling power in the rested contralateral leg.

Methods

Participants

Twelve endurance trained male cyclists (age: 26 ± 4 yr; body mass: 78 ± 9 kg; height: 1.83 ± 0.06 m; maximal oxygen consumption (VO_{2max}): 61 ± 7 ml kg^{-1} min^{-1}) volunteered to participate in this investigation. Participants had regularly trained in cycling for 6 ± 3 yr. At the time of study, participants were training 11 ± 3 h wk^{-1} and competing in local road cycling, triathlon, and/or mountain bike events. Experimental procedures were reviewed by the University of Utah Institutional Review Board and all participants provided written informed consent prior to testing.

Experimental protocol

At preliminary visits to the laboratory, participants performed familiarization trials of maximal single-leg cycling and maximal isometric handgrip trials. Participants also performed practice intervals of submaximal single-leg cycling and an incremental

cycling test (13) for determination of VO_{2max}. During the experimental week participants reported to the laboratory on two separate days to perform: 1) fatigued ipsilateral leg or 2) rested contralateral leg cycling protocol, which are described below and also illustrated in Figure 3.1. The fatigued ispilateral leg and rested contralateral leg cycling protocols were performed in a counter-balanced order. Experimental visits were separated by a least 48 h and were completed at the same time of day. Participants were instructed to avoid vigorous exercise 24 h before each experimental visit.

For the fatigued ipsilateral leg cycling protocol participants performed a 5 min single-leg cycling warm-up with their right leg followed by a maximal single-leg cycling trial (4.5 s) with their right leg. Subsequently, participants rested for 15 minutes and then again performed a maximal single-leg cycling trial with their right leg. Participants then performed a 5 min single-leg cycling warm-up with their right leg followed by 10 min maximal effort single-leg cycling time trial (TT) with their right leg. Within 30 s after the TT, participants performed a maximal single-leg cycling trial with their right leg. Maximal cycling trials were also performed at 3, 5, and 10 min post-TT with the right leg. Immediately following each pre- and post-TT maximal cycling trial, participants performed a maximal isometric handgrip trial with their right arm.

For the rested contralateral leg cycling protocol participants performed a 5 min single-leg cycling warm-up with their right leg followed by a maximal single-leg cycling trial (4.5 s) with their right leg. Subsequently, participants rested for 15 minutes and then again performed a maximal single-leg cycling trial with their right leg. Participants then performed a 5 min single-leg cycling warm-up with their left leg followed by 10 min maximal effort single-leg cycling TT with their left leg. Within 30 s after the TT,

participants performed a maximal single-leg cycling trial with their right leg. Maximal cycling trials were also performed at 3, 5, and 10 min post-TT with the right leg. Immediately following each pre- and post-TT maximal cycling trial, participants performed a maximal isometric handgrip trial with their right arm.

Maximal single-leg cycling

Participants performed maximal single-leg cycling trials (4.5 s) with their right leg on an inertial-load cycle ergometer (61). Participants were instructed to remain seated throughout each trial and were given standardized verbal encouragement. The ergometer was fitted with racing handlebars, cranks, and saddle, and fixed to the floor and participants wore cycling shoes that locked onto the pedal (Speedplay Inc., San Diego, CA, USA). A 97 N counterweight was attached to the contralateral ergometer crank to facilitate smooth single-leg cycling and the foot of the non-exercising leg was secured to a stabilization platform. Inertial-load method determines maximal power across a range of pedaling rates (e.g., 60-180 rpm) in a single brief trial. These methods have been previously described by Martin and colleagues (61). Briefly, participants began each trial from rest and accelerated maximally for eight pedal revolutions with resistance provided solely by the moment of inertia of the flywheel. Angular position data were low pass filtered at 8 Hz using a 5^{th} order spline (88) and angular velocity and acceleration were determined from the spline coefficients. Torque averaged over each complete crank revolution was calculated as the rate of change in angular momentum. For each trial, torque-pedaling rate relationship was determined and linear extrapolation was performed to obtain values for maximum torque (i.e., isometric) and maximum pedaling rate. Power averaged over each complete crank revolution was calculated as

rate of change in kinetic energy and maximum power was the highest value during each trial. For each trial, the power-pedaling rate relationship was determined and the optimal pedaling rate that elicited maximum power was also identified.

Single-leg cycling time trial

Participants performed a 10 min maximal effort single-leg cycling TT with their right or left leg on a Monark friction-braked cycle ergometer (Vansbro, Sweden). Before the TT, participants were instructed to cycle as "hard as you can go" in order to produce the greatest amount of power and were given standardized verbal encouragement throughout the TT. Participants were also instructed to maintain the same pedaling rate for each TT (e.g., 90 rpm). A high-powered industrial fan was placed near the participants in order to keep them cool. The ergometer was fitted with racing handlebars, cranks, and saddle, and fixed to the floor and participants wore cycling shoes that locked onto the pedal (Speedplay Inc., San Diego, CA, USA). As described above a counterweight was attached to the contralateral ergometer crank to facilitate smooth single-leg cycling. Mean power produced during each TT was quantified using a power meter (Schoberer Rad Messtechnik, SRM, Jülich, Germany) that collected data at 2 Hz. Note that previous authors (2, 47, 60) have reported that the SRM powermeter provides accurate measurements of power during high-intensity cycling. During the final 30 s of the TT overall rating of perceived exertion ($RPE_{overall}$) and specific leg perceived exertion (RPE_{legs}) were assessed using a Borg 6-20 scale (22). Heart rate (Polar CS300, Kempele, Finland) was also assessed during the final 30 s of the TT. Whole blood lactate (ARKRAY Lactate Pro LT-1710, Kyoto, Japan) was measured 90 s post-TT.

Maximal isometric handgrip

Participants performed a maximal isometric hand grip trial (3 s) with their right hand using a hydraulic handgrip dynamometer (Smith & Nephew Rehabilitation, Memphis, TN, USA). Participants were instructed to squeeze the device with maximal effort while maintaining a 90° elbow angle. Standardized verbal encouragement was provided during each trial.

Quantification of fatigue

To quantify exercise-induced fatigue, we compared pre- to post-TT changes in maximum cycling power of the fatigued ipsilateral leg. To evaluate potential cross-over effects of fatigue, we compared pre- to post-TT changes in maximum cycling power of the rested contralateral leg. It is important to note that the rested contralateral leg was passive during the TT and was likely not warmed-up prior to the post-TT maximal cycling trials. Thus, potential reductions in maximum cycling power of the rested contralateral leg might be influenced by changes in muscle temperature (76). Therefore, to account for possible temperature effects, we included a pre-TT maximal cycling trial that was preceded by a 5 min warm-up (pre-TT_{warm}) and an additional pre-TT maximal cycling trial that was preceded by 15 min of rest (i.e., no warm-up, pre-TT_{cold}). If maximum power was lower when performed without a warm-up, pre-TT_{cold} trial was used for the pre- to post-TT comparison for the rested contralateral leg only. Finally, we also evaluated pre- to post-TT changes in maximum isometric handgrip force to determine if exercised-induced fatigue altered neuromuscular function in rested muscles of the upper limbs.

Data analysis

A two-way repeated measures analysis of variance (ANOVA) was performed to assess differences in maximum power between pre-TT_{warm} and pre-TT_{cold} maximal cycling trials. Separate student's paired t-tests were used to assess differences in power, heart rate, lactate, RPE_{body}, and RPE_{legs} between the right (fatigued ispilateral leg cycling protocol) and left (rested contralateral leg cycling protocol) leg TT's. Separate two-way repeated measures ANOVA procedures were used to compare pre- to post-TT changes in dependent variables (maximum power, maximum isometric torque, optimal pedaling rate, maximum pedaling rate, and maximum isometric handgrip force). If any of the ANOVA's were significant, then subsequent post hoc procedures (Fisher least significant differences) were performed to determine where those differences occurred. Data were presented as mean ± standard error of the mean (SEM) and initial alpha was set to 0.05.

Results

Maximum cycling power produced during the pre-TT_{cold} trial was reduced by 5 ± 3% compared to pre-TT_{warm} (626 ± 34 vs. 597 ± 34 W, $P < 0.01$, Figure 3.2). Thus, pre-TT_{cold} values were used for all subsequent pre- to post-TT comparisons for the rested contralateral leg only. In contrast, pre-TT_{warm} values were used for the pre- to post-TT comparisons for fatigued ipsilateral. Power, heart rate, blood lactate, and RPE assessed during the right (fatigued ispilateral leg cycling protocol) and left (rested contralateral leg cycling protocol) leg TT's did not differ (Table 3.1). Compared to pre-TT, maximum cycling power produced by the fatigued ipsilateral leg was reduced by 22 ± 3% at 30 s post-TT and remained reduced by 9 ± 2% at 5 min post-TT (both $P < 0.05$, Figure 3.3, Table 3.2). Post-TT maximum cycling power produced by the rested contralateral leg did

not differ from pre-TT values ($P = 0.90$, Figure 3.3, Table 3.2). Compared to pre-TT, maximum isometric torque generated by the fatigued ipsilateral leg was reduced by 20 ± 2% at 30 s post-TT and remained reduced by 4 ± 2% at 10 min post-TT (both $P < 0.05$, Table 3.2). There were no changes in maximum isometric torque produced by the rested contralateral leg ($P = 0.14$, Table 3.2). Complete torque-pedaling rate and power-pedaling rate relationships are illustrated in Figure 3.4. The repeated measures ANOVA procedures indicated significant main effects of time for optimal pedaling rate and maximum pedaling rate as these variables were increased at 5 and 10 min post-TT ($P < 0.05$, Table 3.2). There were no alterations in maximum isometric handgrip force ($P = 0.10$, pre-TT: 534 ± 22, post-TT 30 s: 540 ± 21, post-TT 3 min: 525 ± 19, post-TT 5 min: 529 ± 20, post-TT 10 min: 547 ± 19 N).

Discussion

In this investigation, we used high intensity single-leg cycling (i.e., 10 min TT) to induce fatigue and subsequently evaluated maximum cycling power of the rested contralateral leg as well as the fatigued ipsilateral leg. Our main finding was that maximum cycling power in the rested contralateral leg was maintained despite considerable power loss in the fatigued ipsilateral leg. These results suggest that any potential cross-over of fatigue, if at all present, was not sufficient to measurably compromise maximum power of the rested contralateral leg when fatigue was induced via high-intensity endurance exercise involving a substantial muscle mass. Additionally, maximum isometric handgrip force was also unaffected by fatigue. Taken together, our results suggest that, following high intensity endurance exercise, compromises in

maximal voluntary neuromuscular function are limited to those muscles involved in the fatiguing locomotor task.

Warm-up effects and quantification of fatigue

An important part of our experimental design was that we included two different pre-TT maximal cycling trials in order to determine the effect of a brief warm-up on maximum cycling power. This was necessary as the rested contralateral leg was passive during the TT and thus not likely warmed-up prior to the post-TT maximal cycling trial. As expected, pre-TT maximum cycling power was reduced in the absence of a warm-up. Based on this finding, we then used the pre-TT maximal cycling trial that was preceded by 15 min of rest (i.e., no warm-up, pre-TT_{cold}) for the pre- to post-TT comparison for the rested contralateral leg. Therefore, any potential changes in maximum cycling power of the rested contralateral leg would be due to a cross-over of fatigue rather than changes in muscle temperature (76). This adjustment, however, was not made for the fatigued ipsilateral leg as this leg was active during the TT and likely sufficiently warmed-up at the time the post-TT maximal cycling trial was conducted. Accordingly, the pre-TT that was preceded by a 5 min cycling warm-up (pre-TT_{warm}) was used for the pre- to post-TT comparison for the fatigued ipsilateral leg.

Exercise-induced fatigue

During the TT, participants were able to produce substantial power with one leg (~200 W) which resulted in heart rate, blood lactate, and RPE responses similar to those associated with high-intensity double-leg cycling (7, 8, 56). Previous authors (1, 24) have demonstrated that high-intensity single-leg cycling permits higher individual leg

power outputs compared to double-leg cycling. Thus, not only did our exercise modality place considerable stress on the whole-body but it also likely increased single-leg exercise intensity and the associated intramuscular metabolic milieu (51). After the TT, maximum power in the fatigued ipsilateral leg was initially reduced by 22% and remained reduced at 5 min post-TT. These results generally support previous reports (16, 56, 77, 89) of 25-32% reductions in maximum double-leg cycling power and indicate that high-intensity single-leg cycling was effective for inducing fatigue in the ipsilateral leg. Finally, exercise-induced fatigue in the ipsilateral leg likely manifested through a combination of central and peripheral mechanisms as several investigators have documented the development of central (17, 34, 79) and peripheral fatigue (7-10, 12, 17, 34, 79) during high-intensity cycling exercise.

Interestingly, reductions in maximum cycling power in the fatigued ipsilateral leg were not associated with significant reductions in optimal or maximum pedaling rate. This could suggest that reductions in maximum power were largely due to reductions in torque-generating capacity. Indeed, maximum isometric torque was reduced by a similar magnitude as maximum power (20%). Together, these data might reflect that reductions in maximum power were possibly due to impairments in force production (i.e., cross-bridge level) rather than reduced muscle shortening velocity (i.e., calcium handling). Our results contrast those of Buttelli and colleagues (26) who reported reductions in maximum pedaling rate without changes in maximum isometric torque following high-intensity constant power cycling. At this time we do not fully understand these contrasting results but differences could be related to the limitations of the ergometer (78) used by Buttelli and colleagues (26). Nonetheless, the results from the present study also

clearly demonstrate that power-pedaling rate relationships maintain their parabolic shape following high-intensity cycling, which has been a recent topic of debate (54, 55, 57, 58).

Potential cross-over of fatigue

In contrast to the reductions in maximum cycling power in the fatigued leg, maximum cycling power was unaffected in the rested contralateral leg. In fact, pre- to post-TT torque-pedaling rate and power-pedaling rate relationships were nearly identical (Figure 3.4). This is quite impressive given that participants were working close to maximal effort and producing substantial power with the ipsilateral leg during the TT. Thus, despite substantial fatigue in the ipsilateral leg, a cross-over of fatigue was either not present or not large enough to measurably impair maximum power of the rested contralateral leg when fatigue was induced via high-intensity endurance exercise involving substantial muscle mass. These results insinuate that output from spinal motor neurons was sufficient to enable participants to generate the same baseline maximum cycling power in the rested contralateral leg. With this in mind, central motor drive to the rested contralateral leg was likely unaffected by fatigue in the ipsilateral leg.

In support of our results, previous authors (72, 85) have reported that fatigue induced via a maximal isometric contraction of a single limb muscle does not impair maximum isometric force in the rested contralateral muscle. Conversely, other authors (62) have reported that sustained isometric knee extensor exercise reduced maximum isometric force in rested contralateral knee extensors by 13%. Such differences could be related to the age and sex of the participants and / or type of task (39) to induce fatigue. Even though there is some variation in these findings, our results along with the *majority* of previous studies (72, 85) indicate that fatigue in a single limb muscle / muscle groups

does not impair maximum voluntary function in the previously rested homologous contralateral muscle / muscle groups.

Our results relating to the absence of a cross-over of fatigue were unanticipated and three alternative explanations are worth mentioning. First, as suggested by Amann and colleagues (7, 10-12), during the TT increased firing of group III and IV muscle afferents from the fatigued ipsilateral leg could have exerted inhibitory influences on central motor drive with the subsequent consequence of limited maximum cycling power in the rested contralateral leg. However, for a brief period, participants may have been able to override this inhibitory feedback and produce the same baseline maximum cycling power in the rested leg. To test this theory it might be very illuminating to also evaluate the extent to which exercise-induced fatigue in the ipsilateral leg impacts high-intensity *endurance* performance in the rested contralateral leg. Second, it is salient to note that participants in this study were endurance trained cyclists and were tested in the middle of the racing season. Competitive cycling is inherently a non-steady-state activity performed with intermittent high cycling powers (71). Further, chronic endurance training and associated increased brain mitochondrial biogenesis could attenuate the development of central fatigue (81). Therefore, cyclists in this study may have been uniquely prepared to perform high intensity single-leg cycling and overcome cross-over fatigue to produce maximum cycling power with the rested contralateral leg. Finally, maximum cycling power in the rested contralateral leg may have been initially reduced but could have recovered prior to the post-TT assessment, as there was a short delay due to ergometer constraints. However, the occurrence of such quick recovery is unlikely

given that previous authors have reported that central fatigue (17, 34, 79) can last for up to several minutes following high intensity cycling.

Limb specificity of fatigue

In this investigation, we also evaluated pre- to post-TT changes in maximum isometric handgrip force in an attempt to determine if a cross-over of fatigue manifested with a "global" impairment in maximum voluntary neuromuscular function. Specifically, central fatigue (45) could be induced by changes in concentrations of circulating neurotransmitters in the brain (32), resulting in reduced neuromuscular function in rested muscles not associated with the fatiguing task. Additionally, humoral factors associated with substantial peripheral fatigue in the ipsilateral leg could have lead to peripheral fatigue in the rested contralateral leg. Although such factors were not directly assessed, the lack of changes in maximum isometric handgrip force as well as maximum power in the rested contralateral leg demonstrate that voluntary neuromuscular function was compromised only in exercised muscles of the fatigued ipsilateral leg. These data also suggest that high intensity single-leg cycling in the ipsilateral leg did not affect participants' motivation to perform subsequent maximal voluntary isometric and dynamic contractions in other previously rested limbs / muscles. Finally, the lack of changes in maximum isometric handgrip force is consistent with previous reports that indicate that maximum isometric handgrip force is maintained after high-intensity cycling (34) and prolonged running (66, 69, 73, 74).

Summary

This is the first investigation to evaluate a potential cross-over of fatigue when fatigue is induced via high-intensity endurance exercise involving a substantial muscle mass. Following the single-leg cycling TT, maximum cycling power in the fatigued ipsilateral leg was substantially reduced and remained reduced for several minutes. Even with substantial fatigue in the ipsilateral leg, participants were still able to produce the same baseline maximum cycling power with the rested contralateral leg. Maximum isometric handgrip force was also unaffected by fatigue. Taken together, these results suggest that fatigue induced via high-intensity endurance exercise in one limb does not impair maximal voluntary neuromuscular function in previously rested limbs / muscles.

Table 3.1: Physiological responses to the single-leg cycling time trial.

	Right Leg	**Left Leg**
Power (W) [a]	203 ± 8	199 ± 8
HR (beats min^{-1}) [b]	177 ± 3	175 ± 4
$RPE_{overall}$ [b]	18.3 ± 0.5	17.7 ± 0.6
RPE_{legs} [b]	19.6 ± 0.1	19.3 ± 0.2
Lactate (mmol L^{-1}) [c]	11.2 ± 0.6	11.5 ± 0.5

Values are reported as Mean ± SEM. Note that the right leg time trial (TT) was part of the fatigued ipsilateral leg protocol and that the left leg TT was part of the rested contralateral leg protocol.

[a] Averaged over 10 min

[b] Assessed during final 30 s

[c] Assessed within 90 s post-TT

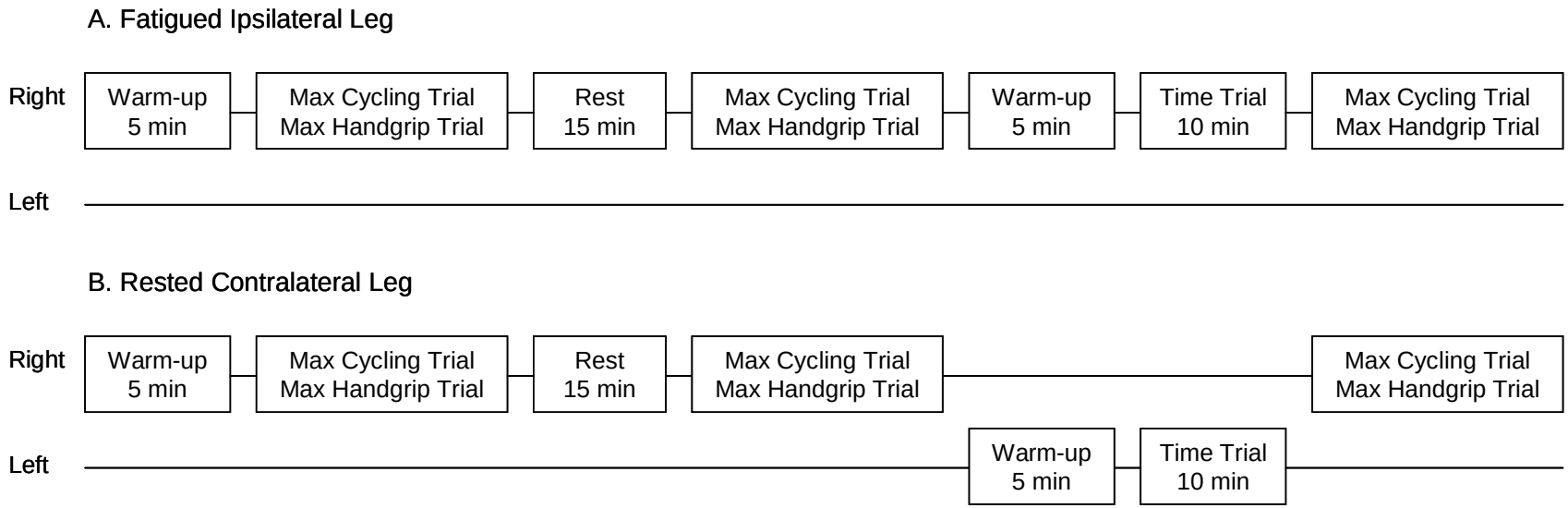

Figure 3.1: Experimental protocol. Schematic illustration of the fatigued ipsilateral (A) and rested contralateral (B) leg protocols. Protocols were administered in a counter balanced fashion. Maximal cycling and isometric handgrip trials were performed at 30 s, 3 min, 5 min, and 10 min post-TT.

Table 3.2: Pre- to post-TT changes in maximal neuromuscular function.

	Fatigued Leg					Rested Leg				
	Pre	**30 s**	**3 min**	**5 min**	**10 min**	**Pre**	**30 s**	**3 min**	**5 min**	**10 min**
P_{max} (W)	627 ± 31	489 ± 30*	561 ± 29*	570 ± 30*	602 ± 33	596 ± 35	597 ± 31	603 ± 32	597 ± 27	596 ± 31
T_{max} (Nm)	101 ± 5	79 ± 5*	89 ± 4*	90 ± 4*	96 ± 4*	99 ± 5	97 ± 4	97 ± 4	94 ± 4	95 ± 4
RPM_{opt} [a]	113 ± 9	109 ± 4	114 ± 3	115 ± 3	114 ± 3	110 ± 2	111 ± 2	114 ± 2	114 ± 2	115 ± 2
RPM_{max} [a]	227 ± 5	218 ± 7	227 ± 5	230 ± 7	231 ± 7	219 ± 4	223 ± 4	228 ± 4	230 ± 4	231 ± 4

Values are reported as Mean ± SEM. P_{max}, maximum cycling power; T_{max}, maximum isometric torque produced at the onset of maximal cycling; RPM_{opt}, optimal pedaling rate that elicited maximum cycling power; RPM_{max}, maximum pedaling rate. Note that rested contralateral leg pre-TT values tended to be lower than fatigued ipsilateral values due to the lack of a cycling warm-up.

* $P < 0.05$ vs. pre-TT

[a] main effect of time ($P < 0.05$)

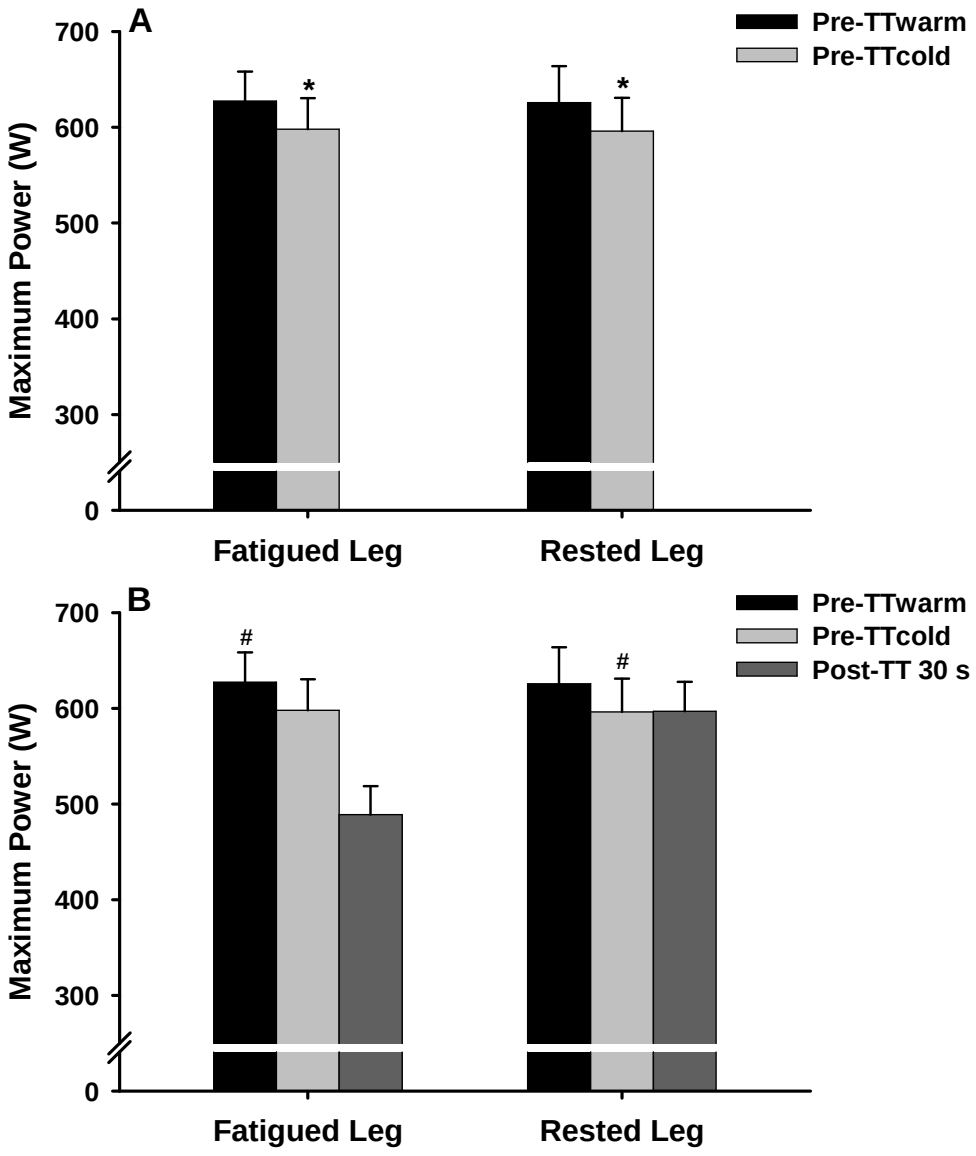

Figure 3.2: Influence of a cycling warm-up. Effect of a warm-up (A) on pre-TT maximum cycling power (mean ± SEM). Pre-TTwarm represents the maximal cycling trial that was preceded by a 5 min cycling warm-up whereas pre-TTcold represents the maximal cycling trial that was preceded by 15 min of rest (i.e., no warm-up). * $P < 0.01$ vs. pre-TTwarm. Graphical illustration of quantification of fatigue (B). # indicates pre-TT maximal cycling trial used for the pre- to post-TT comparison.

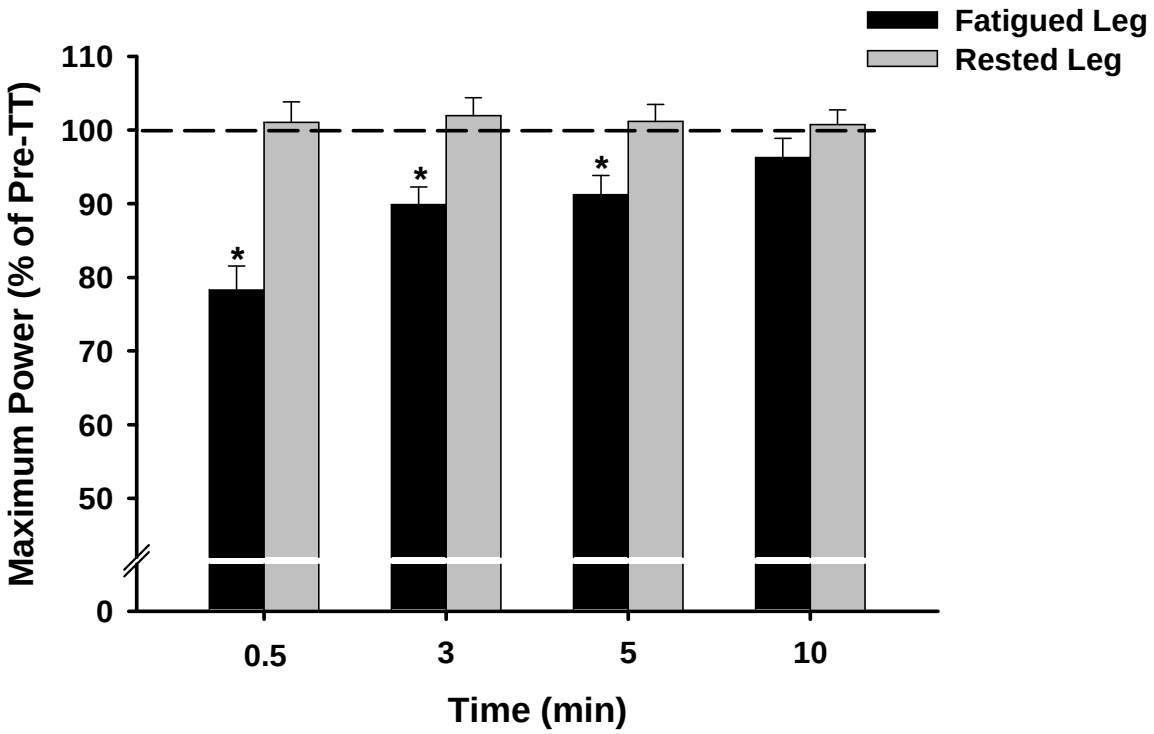

Figure 3.3: Alterations in maximum cycling power. Relative pre- to post-TT changes in maximum cycling power (mean ± SEM) for the fatigued ipsilateral and rested contralateral leg. * $P < 0.05$ compared to pre-TT (dotted line).

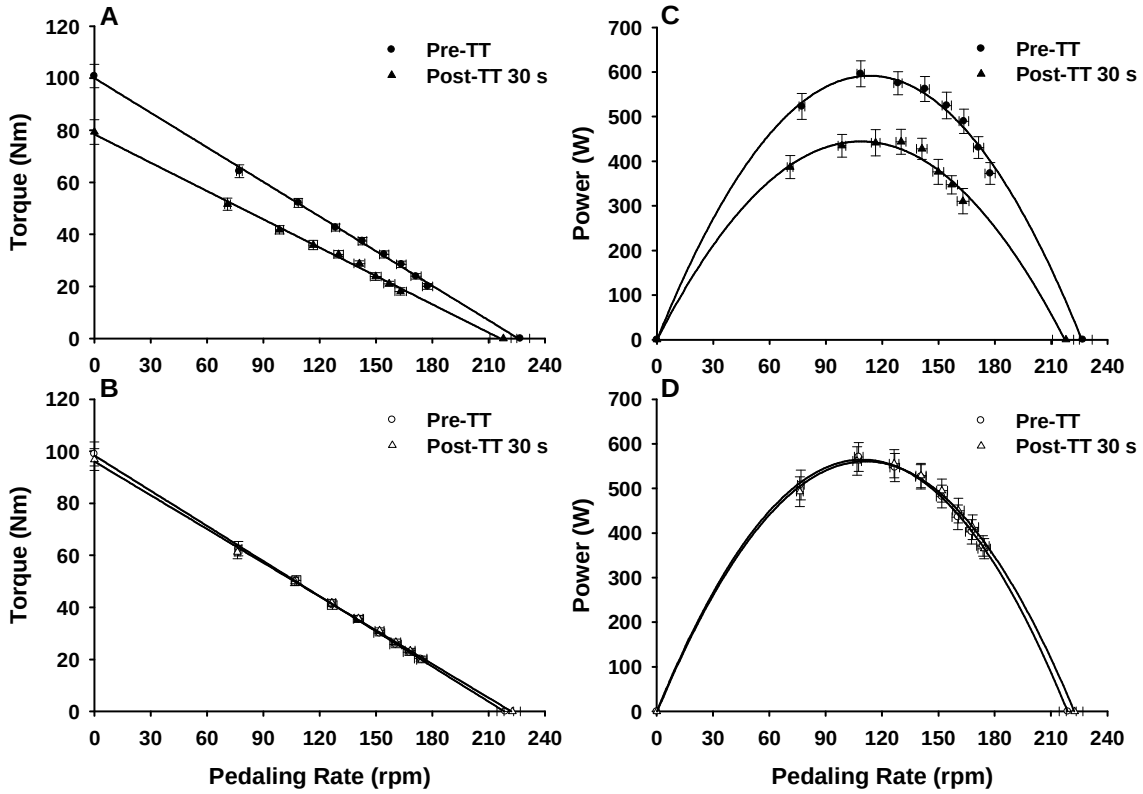

Figure 3.4: Torque- and power-pedaling rate relationships. Maximal cycling torque-pedaling rate (A, B) and power-pedaling rate (C, D) relationships for the fatigued ipsilateral (closed symbols) and rested contralateral leg (open symbols). Maximum isometric torque and maximum power were reduced for the fatigued ipsilateral leg at 30 s post-TT, but did not change for the rested contralateral leg. Data are presented as mean ± SEM.

4. EFFECTS OF AGING ON THE DEVELOPMENT OF FUNCTIONAL CONSEQUENCES OF CENTRAL AND PERIPHERAL FATIGUE DURING SINGLE-LEG CYCLING

The ability to produce muscular force / power and resist the development of fatigue is important when performing functional activities for prolonged periods of time. Recently, Christie and colleagues (28) performed a systematic review and meta analysis of muscle fatigue and aging and reported that older individuals develop less fatigue than younger individuals *during isometric* muscle contractions. However, *during dynamic* muscle contractions older individuals exhibit greater fatigue (i.e., power loss) compared to younger individuals. These authors also emphasized the need for additional research to evaluate age-related differences in fatigue particularly during dynamic exercise as production of muscular power is important for maintaining physical function and independence with advanced age (14, 44) .

Exercise-induced fatigue, a reversible reduction in the force- and power-generating ability of the neuromuscular system (19, 43), can manifest through central (45) and / or peripheral (4) mechanisms. Traditionally, the development of central fatigue is evaluated during a maximal isometric contraction. Similarly, exercise-induced peripheral muscle fatigue is often quantified via the reduction in force output in response to direct electric / magnetic motor nerve stimulation shortly after intense muscle contractions. Insight into central and peripheral aspects of fatigue can help to explain

age-related differences in fatigue resistance (5, 15, 20, 27, 31, 36, 49, 80). However, it can be challenging to separate the relative contributions of central and peripheral fatigue *during dynamic* muscle contractions as traditional techniques are difficult to utilize. Indeed, Kent-Braun and colleagues (50) emphasized that, "Currently, the relative importance of central and peripheral factors in fatigue during dynamic contractions in the elderly is not known."

The functional impact of central and peripheral fatigue on dynamic neuromuscular function could be approximated by using a single-leg cycling model. That is, high-intensity single-leg cycling could be used to induce peripheral fatigue in the working leg while possibly facilitating central fatigue. Subsequent evaluation of maximum cycling power in the rested contralateral leg and fatigued ipsilateral leg offers a paradigm for examining the functional impact of central and peripheral fatigue during dynamic exercise that involves the large muscle mass of the legs. For example, if maximum cycling power was reduced in the fatigued ipsilateral leg, this would likely represent a combination of central and peripheral fatigue as previous investigators have documented the development of central (17, 34, 79) and peripheral (7-10, 12, 17, 34, 79) fatigue during high-intensity double-leg cycling. Additionally, if maximum cycling power was reduced in the rested contralateral leg, this fatigue would most likely be central in origin (62, 72, 85) with peripheral factors playing a lesser role (62).

Age-related changes in functional capacity may be attributed in part to reduced physical activity and sedentary lifestyle. Indeed, many of the so called aging effects occur to a lesser extent in middle-age to older adults who strive to maintain and even improve athletic performance (i.e., masters athletes) (29, 41, 53, 70). Thus, masters

athletes offer a unique model of highly active aging (82, 83). In the context of fatigue, masters athletes, particularly masters cyclists, may be an interesting group to study. Specifically, competitive cycling is inherently a non-steady state activity performed with intermittent high net cycling powers (71) and such lifelong training may help to preserve the ability of the neuromuscular system to resist the development of fatigue.

Our purpose for conducting this investigation was to evaluate the effects of aging on the development of functional consequences of central and peripheral fatigue induced via dynamic exercise involving a large muscle mass. Specifically, we determined the extent to which high-intensity single-leg cycling altered maximum cycling power of the: 1) fatigued ipsilateral and 2) rested contralateral leg. Previous results (15, 30, 64, 68) from dynamic tasks involving a small muscle mass suggest that older adults would exhibit greater fatigue compared to young adults. However, lifelong endurance training in masters cyclists could potentially attenuate the development of fatigue associated with aging. Therefore, we hypothesized that masters cyclists would exhibit similar levels of fatigue compared to young cyclists.

Methods

Participants

Twelve endurance trained young cyclists (age: 18-30 yr) and 12 masters cyclists (age: 50-65 yr) volunteered for this study. Cyclists were recruited from local cycling clubs in the community. Participant demographics along with self-reported training data are presented in Table 1. Experimental procedures were reviewed by the University of Utah Institutional Review Board and all participants provided written informed consent prior to testing.

Experimental protocol

At preliminary visits to the laboratory, participants performed familiarization trials of maximal single-leg cycling and maximal isometric handgrip trials. Participants also performed practice intervals of submaximal single-leg cycling and an incremental double-leg cycling test (13) for determination of VO_{2max}. During the experimental week participants reported to the laboratory on two separate days to perform: 1) fatigued ipsilateral leg or 2) rested contralateral leg cycling protocol which are described below and also illustrated in Figure 3.1. The fatigued ispilateral leg and rested contralateral leg cycling protocols were performed in a counter-balanced order. Experimental visits were separated by a least 48 h and were completed at the same time of day. Participants were instructed to avoid vigorous exercise 24 h before each experimental visit.

For the fatigued ipsilateral leg cycling protocol participants performed a 5 min single-leg cycling warm-up with their right leg followed by a maximal single-leg cycling trial (4.5 s) with their right leg. Subsequently, participants rested for 15 minutes and then again performed a maximal single-leg cycling trial with their right leg. Participants then performed a 5 min single-leg cycling warm-up with their right leg followed by 10 min maximal effort single-leg cycling time trial (TT) with their right leg. Within 30 s after the TT, participants performed a maximal single-leg cycling trial with their right leg. Maximal cycling trials were also performed at 3, 5, and 10 min post-TT with the right leg. Immediately following each pre- and post-TT maximal cycling trial, participants performed a maximal isometric handgrip trial with their right arm.

For the rested contralateral leg cycling protocol participants performed a 5 min single-leg cycling warm-up with their right leg followed by a maximal single-leg cycling

trial (4.5 s) with their right leg. Subsequently, participants rested for 15 minutes and then again performed a maximal single-leg cycling trial with their right leg. Participants then performed a 5 min single-leg cycling warm-up with their left leg followed by 10 min maximal effort single-leg cycling TT with their left leg. Within 30 s after the TT, participants performed a maximal single-leg cycling trial with their right leg. Maximal cycling trials were also performed at 3, 5, and 10 min post-TT with the right leg. Immediately following each pre- and post-TT maximal cycling trial, participants performed a maximal isometric handgrip trial with their right arm.

Maximal single-leg cycling

Participants performed maximal single-leg cycling trials (4.5 s) with their right leg on an inertial-load cycle ergometer (61). Participants were instructed to remain seated throughout each trial and given standardized verbal encouragement. The ergometer was fitted with racing handlebars, cranks, and saddle, and fixed to the floor and participants wore cycling shoes that locked onto the pedal (Speedplay Inc., San Diego, CA, USA). A 97 N counterweight was attached to the contralateral ergometer crank to facilitate smooth single-leg cycling and the foot of the non-exercising leg was secured to a stabilization platform. Inertial-load method determines maximal power across a range of pedaling rates (e.g., 60-180 rpm) in a single brief trial. These methods have been previously described by Martin and colleagues (61). Briefly, participants began each trial from rest and accelerated maximally for eight pedal revolutions with resistance provided solely by the moment of inertia of the flywheel. Angular position data were low pass filtered at 8 Hz using a 5^{th} order spline (88) and angular velocity and acceleration were determined from the spline coefficients. Power averaged over each

complete crank revolution was calculated as the rate of change in kinetic energy and maximum power was the highest value during each trial. For each trial, the power-pedaling rate relationship was determined and the optimal pedaling rate that elicited maximum power was also identified. Note that optimal pedaling rate has been reported to be highly related to muscle fiber type (48) and thus may serve as a surrogate measure of muscle fiber type distribution.

Single-leg cycling time trial

Participants performed a 10 min maximal effort single-leg cycling TT with their right or left leg on a Monark friction-braked cycle ergometer (Vansbro, Sweden). Before the TT, participants were instructed to cycle as "hard as you can go" in order to produce the greatest amount of power and were given standardized verbal encouragement throughout the TT. Participants were also instructed to maintain the same pedaling rate for each TT (e.g., 90 rpm). A high-powered industrial fan was placed near the participants in order to keep them cool. The ergometer was fitted with racing handlebars, cranks, and saddle, and fixed to the floor and participants wore cycling shoes that locked onto the pedal (Speedplay Inc., San Diego, CA, USA). As described above a counterweight was attached to the contralateral ergometer crank to facilitate smooth single-leg cycling. Mean power produced during each TT was quantified using a power meter (Schoberer Rad Messtechnik, SRM, Jülich, Germany) that collected data at 2 Hz. Note that previous authors (2, 47, 60) have reported that the SRM power meter provides accurate measurements of power during high-intensity cycling. During the final 30 s of the TT overall rating of perceived exertion ($RPE_{overall}$) and specific leg perceived exertion (RPE_{legs}) were assessed using a Borg 6-20 scale (22). Heart rate (Polar CS300, Kempele,

Finland) was also assessed during the final 30 s of the TT. Whole blood lactate (ARKRAY Lactate Pro LT-1710, Kyoto, Japan) was measured 90 s post-TT.

Maximal isometric handgrip

Participants performed a maximal isometric hand grip trial (3 s) with their right hand using a hydraulic handgrip dynamometer (Smith & Nephew Rehabilitation, Memphis, TN, USA). Participants were instructed to squeeze the device with maximal effort while maintaining a 90° elbow angle. Standardized verbal encouragement was provided during each trial.

Quantification of fatigue

To quantify exercise-induced fatigue, we compared pre- to post-TT changes in maximum cycling power of the fatigued ipsilateral leg. To evaluate potential effects of central fatigue, we compared pre- to post-TT changes in maximum cycling power of the rested contralateral leg. It is important to note that the rested contralateral leg was passive during the TT and was not likely warmed-up prior to the post-TT maximal cycling trials. Thus, potential reductions in maximum cycling power of the rested contralateral leg might be influenced by changes in muscle temperature (76). To account for possible temperature effects, we included a pre-TT maximal cycling trial that was preceded by a 5 min warm-up (pre-TT_{warm}) and an additional pre-TT maximal cycling trial that was preceded by 15 min of rest (i.e., no warm-up, pre-TT_{cold}). If maximum power was reduced in the absence of a warm-up, then the pre-TT_{cold} trial was used for the pre- to post-TT comparison for the rested contralateral leg only. Finally, we also evaluated pre- to post-TT changes in maximum isometric handgrip force to determine if

exercised-induced fatigue altered neuromuscular function in rested muscles of the upper limbs.

Data analysis

Separate independent t-tests were used to compare differences in demographic and training data between the young and masters cyclists. A two-way mixed repeated measures analysis of variance (ANOVA) was performed to assess differences in maximum power between pre-TT_{warm} and pre-TT_{cold} maximal cycling trials. Two-way mixed repeated measures ANOVA procedures were also used to assess differences in power, heart rate, lactate, RPE_{body} and RPE_{legs} between the right (fatigued ispilateral leg cycling protocol) and left (rested contralateral leg cycling protocol) leg TT's. Pre- to post-TT changes in dependent variables (maximum cycling power and maximum isometric handgrip force) were compared using two-way repeated measures ANOVA procedures. If any of the ANOVA procedures were significant, then subsequent post hoc procedures (Fisher least significant differences) were performed to determine where those differences occurred. Data were presented as mean ± standard error of the mean (SEM) and initial alpha was set to 0.05.

Results

Demographic and training characteristics

The older masters cyclists were less massive, had lower VO_{2max} values, and had been training longer compared to young cyclists ($P < 0.05$, Table 4.1). Young and masters cyclists were similar in height and weekly training hours (Table 4.1).

Warm-up effects

During pre-TT_{warm} maximal single-leg cycling trials, masters cyclists were less powerful compared to young (523 ± 31 vs. 626 ± 34 W, age group effect, $P < 0.01$) but this difference was eliminated when power was normalized to body mass (7.2 ± 0.4 vs. 8.1 ± 0.4 W kg^{-1}, $P = 0.13$). Optimal pedaling rate that elicited maximum cycling power during pre-TT_{warm} did not differ between the young and masters cyclists (113 ± 2 vs. 109 ± 2 rpm, $P = 0.29$). Compared to pre-TT_{warm}, maximum cycling power produced during pre-TT_{cold} trials was reduced by 5 ± 1% for young and masters cyclists (trial effect, $P < 0.001$, Figure 4.1) with no interaction of age group ($P = 0.75$). Thus, pre-TT_{cold} values were used for all subsequent pre- to post-TT comparisons for the rested contralateral leg whereas pre-TT_{warm} values were used for pre- to post-TT comparisons for the fatigued ipsilateral leg whereas (Figure 4.1).

Time trials

Mean power produced during the 10 min right (fatigued ipsilateral leg protocol) and left (rested contralateral leg protocol) leg TT's was lower for masters cyclists compared to young (age group effect, $P = 0.05$, Table 4.2). However, this difference was eliminated when mean TT power was scaled to body mass ($P = 0.47$, Table 4.2). Mean TT powers for the right and left leg TT did not differ ($P = 0.75$). Mean pedaling rate was similar for young and masters cyclists ($P = 0.34$) and did not differ between the right and left leg TT's ($P = 0.08$, Table 4.2). Heart rate values were lower for masters cyclists compared to young (age group effect, $P < 0.01$, Table 4.2) but did not differ between the right and left leg TT's ($P = 0.46$). There was a significant leg x age group interaction for $RPE_{overall}$ and RPE_{legs} ($P < 0.05$, Table 4.2). Whole blood lactate values for young and

masters cyclists were similar (P = 0.33) and did not differ between the right and left leg TT's (P = 0.20, Table 4.2).

Pre- to post-TT changes in neuromuscular function

Compared to pre-TT, maximum cycling power produced by the fatigued ipsilateral leg was reduced for young and masters cyclists (time effect, P < 0.01) with no interaction of age group (P = 0.48). In fact, young and masters cyclists exhibited nearly identical levels of fatigue as maximum cycling power in the fatigued ispilateral leg was initially reduced by 22 ± 3 and 21 ± 3% at 30 s post-TT, respectively (Figure 4.2). At 10 min post-TT, maximum cycling power was similar to pre-TT values for both young and masters cyclists (P = 0.06, Figure 4.2). Post-TT maximum cycling power produced by the rested contralateral leg did not differ from pre-TT values for young and masters cyclists (P = 0.45, Figure 4.2). Complete power-pedaling rate relationships for the fatigued ispilateral and rested contralateral leg are illustrated in Figure 4.3. Maximum isometric handgrip force was lower for masters cyclists (P = 0.01) and increased for both groups at 10 min post-TT only (time effect, P < 0.05).

Discussion

In this investigation, we tested the hypothesis that older masters cyclists would exhibit similar levels of fatigue compared to young cyclists when matched for training volume. Our results indicate that power loss and recovery in the fatigued ipsilateral leg were nearly identical for young and masters cyclists. Despite considerable fatigue in the ipsilateral leg, both young and masters cyclists were able to maintain maximum cycling power in the rested contralateral leg. Thus, a cross-over of fatigue (possibly central in origin) was either not present or not large enough to impair maximum cycling power in the

rested contralateral leg. In addition, maximum isometric handgrip force was also unaffected by fatigue. Together, these results indicate that fatigue induced via high-intensity cycling has similar functional consequences for endurance trained young and masters cyclists. These results also suggest that for both groups of cyclists, maximal voluntary neuromuscular function was compromised only in those muscles / muscle groups involved in the fatiguing task. These data support our hypothesis and likely represent a best case scenario for highly active aging.

Warm-up effects

As expected pre-TT maximum cycling power was reduced in the absence of a warm-up for both young and masters cyclists. Based on this finding we then used the pre-TT maximal cycling trial that was preceded by 15 min of rest (i.e., no warm-up, pre-TT_{cold}) for the pre- to post-TT comparison for the rested contralateral leg only. Therefore, any potential changes in maximum cycling power of the rested contralateral leg would be due to fatigue that was likely central in origin rather than changes in muscle temperature (76). For the fatigued ipsilateral leg, pre-TT maximal cycling trial that was preceded by a 5 min cycling warm-up (pre-TT_{warm}) was used for the pre- to post-TT comparison as this leg was active during the TT and likely sufficiently warmed-up prior to the post-TT maximal cycling trials.

Exercise-induced fatigue

After the TT, young and masters cyclists exhibited virtually identical levels of fatigue as maximum cycling power in the fatigued ispilateral leg was initially reduced by 22% and 21%, respectively, and remained reduced at 5 min post-TT. Indeed, relative

pre- to post-TT power-pedaling rate relationships tended to converge onto a single curve (Figure 4.3). These results indicate that high-intensity single-leg cycling was effective for inducing fatigue in the ipsilateral leg and are well supported as several authors (16, 56, 77, 89) have reported similar reductions in maximum cycling power (25-32%) after high-intensity double-leg cycling. Further, exercise-induced fatigue in the ipsilateral leg likely manifested through a combination of central and peripheral mechanisms as several investigators have documented the development of central (17, 34, 79) and peripheral fatigue (7-10, 12, 17, 34, 79) following short-duration high-intensity cycling.

In contrast to the reductions in maximum cycling power in the fatigued leg, maximum cycling power was unaffected in the rested contralateral leg for both young and masters cyclists. This is quite impressive given that participants were working close to maximal effort and producing substantial power with the ipsilateral leg during the TT. These results suggest that a cross-over of fatigue that was possibly central in origin (62) was either not present or not large enough to impair maximum cycling power in the rested leg. In addition, these data provide evidence that output from spinal motor neurons was sufficient to enable both groups of cyclists to generate the same baseline maximum cycling power in the rested contralateral leg. With this in mind, central motor drive to the rested contralateral leg was likely unaffected by fatigue in the isilateral leg.

Collectively, these results indicate that young and masters cyclists developed similar levels of fatigue and recovery following high-intensity endurance exercise involving a substantial muscle mass. Previous authors (15, 30, 64, 68) have reported that older individuals exhibit greater power loss and fatigue compared to younger individuals when fatigue is induced via dynamic exercise involving a small muscle mass. On the other hand, others (52) have reported that older adults develop less fatigue compared to

their younger counterparts whereas others (27) have observed no age-related differences in fatigue. Thus, previous findings relating to age-related differences in fatigue are widely varied. These dissimilar findings could be related to the type of task to induce fatigue and muscle group evaluated. Although it is difficult to directly compare the results from the present study to previous investigations, our results representing similar levels of fatigue come down squarely in the middle of these various reported responses.

Central and peripheral factors

To the best of our knowledge, we are one of the first groups to evaluate functional consequences of central and peripheral aspects of fatigue during dynamic exercise. Our results of similar power loss in the fatigued ipsilateral leg along with the lack of changes in the rested contralateral legs suggest that central and peripheral fatigue likely had similar functional consequences for endurance trained young and masters cyclists when fatigue was induced via high-intensity cycling. Using traditional methods, previous authors (20, 80) have reported greater reductions in voluntary muscle activation (65) during maximal isometric contractions in older individuals suggesting that central fatigue mechanisms contributed to age-related differences in fatigue resistance. However, other authors (5, 15, 27, 31, 36, 49) have reported no differences in central activation suggesting that peripheral fatigue mechanisms likely contributed to age-related differences in fatigue resistance. Once again previous findings are widely varied as fatigue can be task-specific and it is difficulty to compare our results to previous results obtained using isometric small muscle mass models. Future research that combines traditional techniques with the model used in this study may help to unify mechanistic and functional fatigue measures.

Masters athlete model

Age-related changes in neuromuscular function can lead to significant reductions in muscular strength and power and ultimately frailty (87). Such changes, however, may be related partly to reduced physical activity and sedentary lifestyle. To investigate the effects of age, without these confounding factors, we compared fatigue responses in young and masters cyclists who were matched for training volume. Not only were these groups matched for training hours, but they had similar maximum cycling and TT cycling power values (adjusted for body mass) as well as optimal pedaling rates, which suggests they had similar muscle fiber type distributions. Therefore, any differences in fatigue responses would most likely result from the > 30 yr difference in age. Our results of similar fatigue responses between young and masters cyclists agree with previous reports that indicate that young and masters endurance athletes demonstrated similar levels of fatigue in knee extensor muscles following 30 min cycling time trial (41) and heavy resistance training (53). Together, these results provide evidence that masters athletes maintain the ability to resist the development of fatigue.

Limb specificity of fatigue

To determine if a exercise-induced fatigue manifested with a "global" impairment in maximum voluntary neuromuscular function, we also evaluated pre- to post-TT changes in maximum isometric handgrip force in an attempt. The lack of changes in maximum isometric handgrip force as well as maximum power in the rested contralateral leg demonstrate that voluntary neuromuscular function was compromised only in exercised muscles of the fatigued ipsilateral leg. These results suggest that high intensity single-leg cycling in the ipsilateral leg did not affect participants' motivation to perform

subsequent maximal voluntary isometric and dynamic contractions in other previously rested limbs / muscles. Further, these results corroborate previous reports that indicate that maximum isometric handgrip force is maintained after high-intensity cycling (34) prolonged running (66, 69, 73, 74).

Summary

In this investigation, we evaluated the effects of aging on the development of fatigue in endurance trained young and masters cyclists. Even with > 30 yr difference in age, masters cyclists exhibited almost identical levels of fatigue compared to young in the fatigued leg (-21 vs. -22%) and also exhibited similar recovery patterns. In addition, both groups had the ability to overcome considerable fatigue in the ipsilateral leg and produce the same baseline maximum cycling power with the rested leg. Likewise, maximal voluntary neuromuscular function was maintained in the upper limb as maximal isometric handgrip force was unaffected by fatigue. Collectively, these results indicate that fatigue induced via high-intensity cycling has similar functional consequences for endurance trained young and masters cyclists and that impairments in maximal voluntary neuromuscular function were specific to those muscles of fatigued ipsilateral leg. Finally, these results likely provide an example of healthy successful aging and should not be extended to the general sedentary population.

Table 4.1: Participant demographics and training profiles.

Group (n = 12)	Age (yr)	Mass (kg)	Height (m)	VO_{2max} (ml kg^{-1} min^{-1})	Years of Training	Weekly Hours
Young	26 ± 4	78 ± 9	1.83 ± 0.06	61 ± 7	6 ± 3	11 ± 2
Masters	57 ± 5*	73 ± 8*	1.75 ± 0.06	54 ± 6*	22 ± 11*	11 ± 3

Values are reported as Mean ± SD.

* $P < 0.05$ vs. young

Table 4.2: Time trial characteristics.

	Right Leg	**Left Leg**
Power (W) [a]		
Young	203 ± 8	199 ± 8
Masters	179 ± 8	181 ± 6
Power (W/kg)		
Young	2.6 ± 0.1	2.6 ± 0.1
Masters	2.5 ± 0.1	2.5 ± 0.1
Pedaling Rate (rpm)		
Young	90 ± 1	89 ± 1
Masters	88 ± 1	88 ± 1
HR (beats min^{-1}) [a]		
Young	177 ± 3	175 ± 4
Masters	163 ± 3	163 ± 4
$RPE_{overall}$ [b]		
Young	18.3 ± 0.5	17.7 ± 0.6
Masters	18.7 ± 0.4	19.0 ± 0.2
RPE_{legs} [b]		
Young	19.6 ± 0.1	19.3 ± 0.2
Masters	19.3 ± 0.2	19.5 ± 0.2
Lactate (mmol L^{-1})		
Young	11.2 ± 0.6	11.5 ± 0.5
Masters	10.3 ± 0.6	11.0 ± 0.5

Values are reported as Mean ± SEM. Note that the right leg time trial (TT) was part of the fatigued ipsilateral leg protocol and that the left leg TT was part of the rested contralateral leg protocol. Power and pedaling rate were averaged over 10 min. Heart rate (HR), $RPE_{overall}$, and RPE_{legs} were assessed during final 30 s. Lactate was assessed within 90 s of the end of the TT.

[a] Main effect of age group ($P < 0.05$)

[b] Leg x age group interaction ($P < 0.05$)

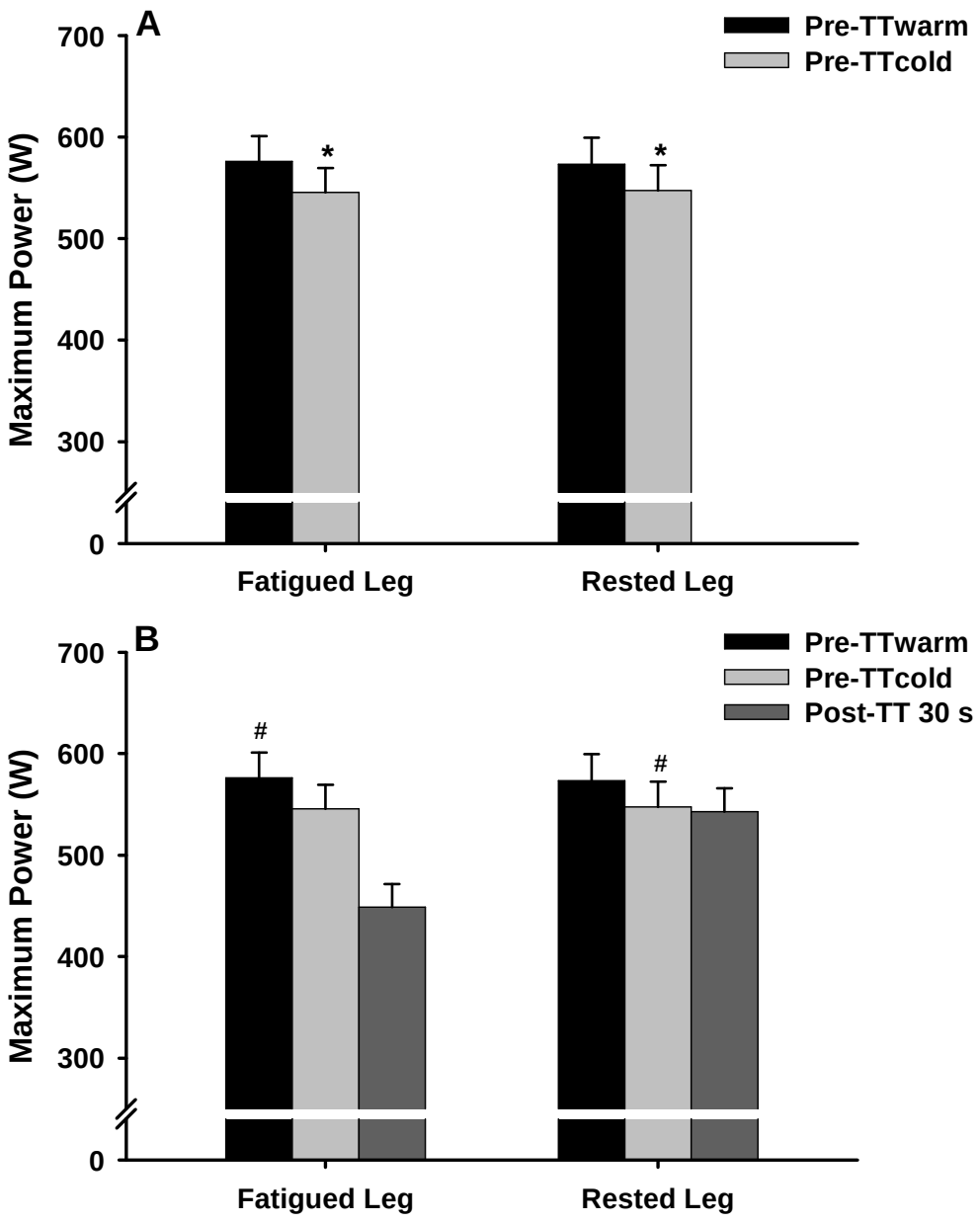

Figure 4.1: Pre-TT maximal cycling and warm-up effects. Effect of a warm-up (A) on pre-TT maximum cycling power. Pre-TTwarm represents the maximal cycling trial that was preceded by a 5 min cycling warm-up whereas pre-TTcold represents the maximal cycling trial that was preceded by 15 min of rest (i.e., no warm-up). Compared to pre-TTwarm, maximum cycling power produced during pre-TTcold trials was reduced by 5 ± 1% for young and masters cyclists (trial effect, * $P < 0.001$) with no interaction of age group. Graphical illustration of quantification of fatigue (B). # indicates pre-TT maximal cycling trial used for the pre- to post-TT comparison for the fatigued ipsilateral and rested contralateral leg. Data are pooled for young and masters cyclists and are presented as mean ± SEM.

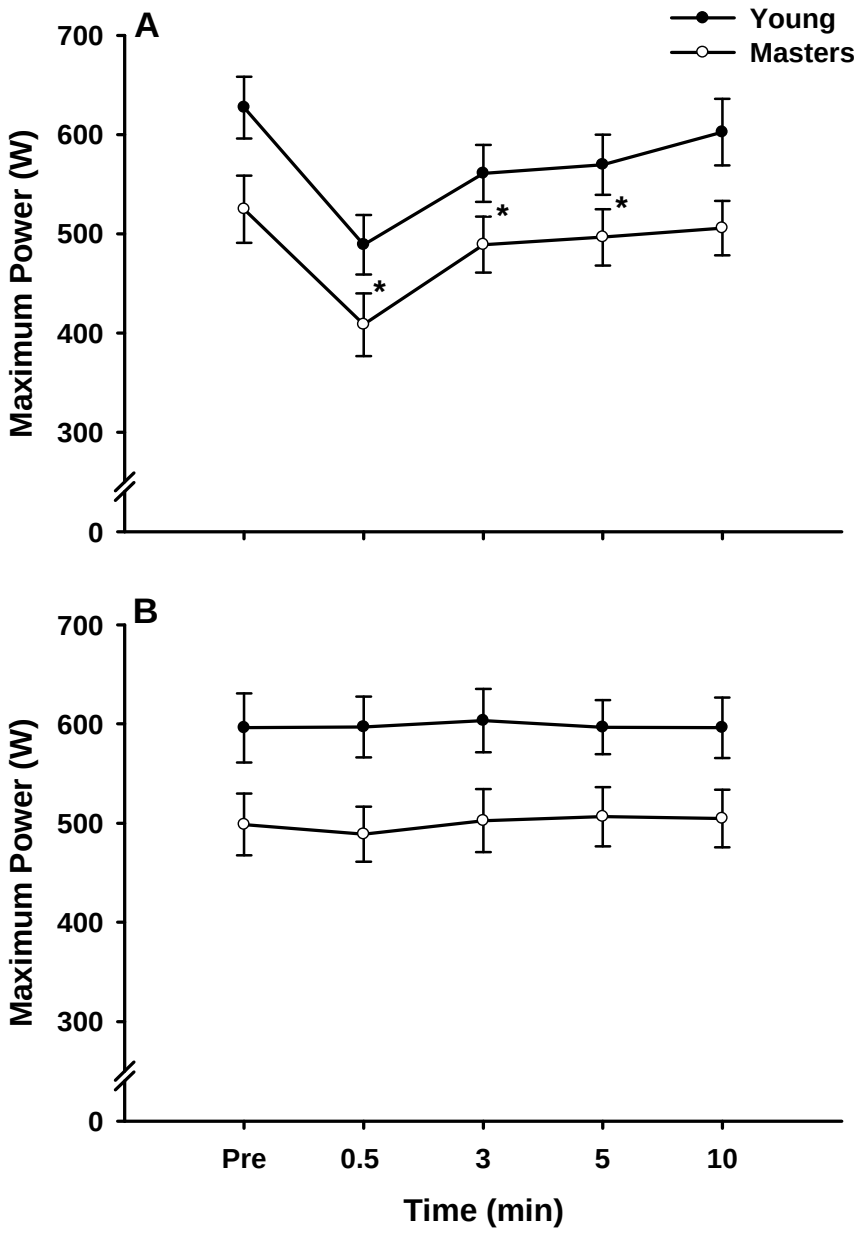

Figure 4.2: Changes in maximum cycling power. Pre- to post-TT changes in maximum cycling power for the fatigued ipsilateral (A) and rested contralateral (B) leg. Compared to pre-TT, maximum cycling power produced by the fatigued ipsilateral leg was reduced at 0.5, 3, and 5 min for young and masters cyclists (time effect, * $P < 0.05$) with no interaction of age group There were no changes in maximum cycling power produced by the rested contralateral leg. Data are presented as mean ± SEM.

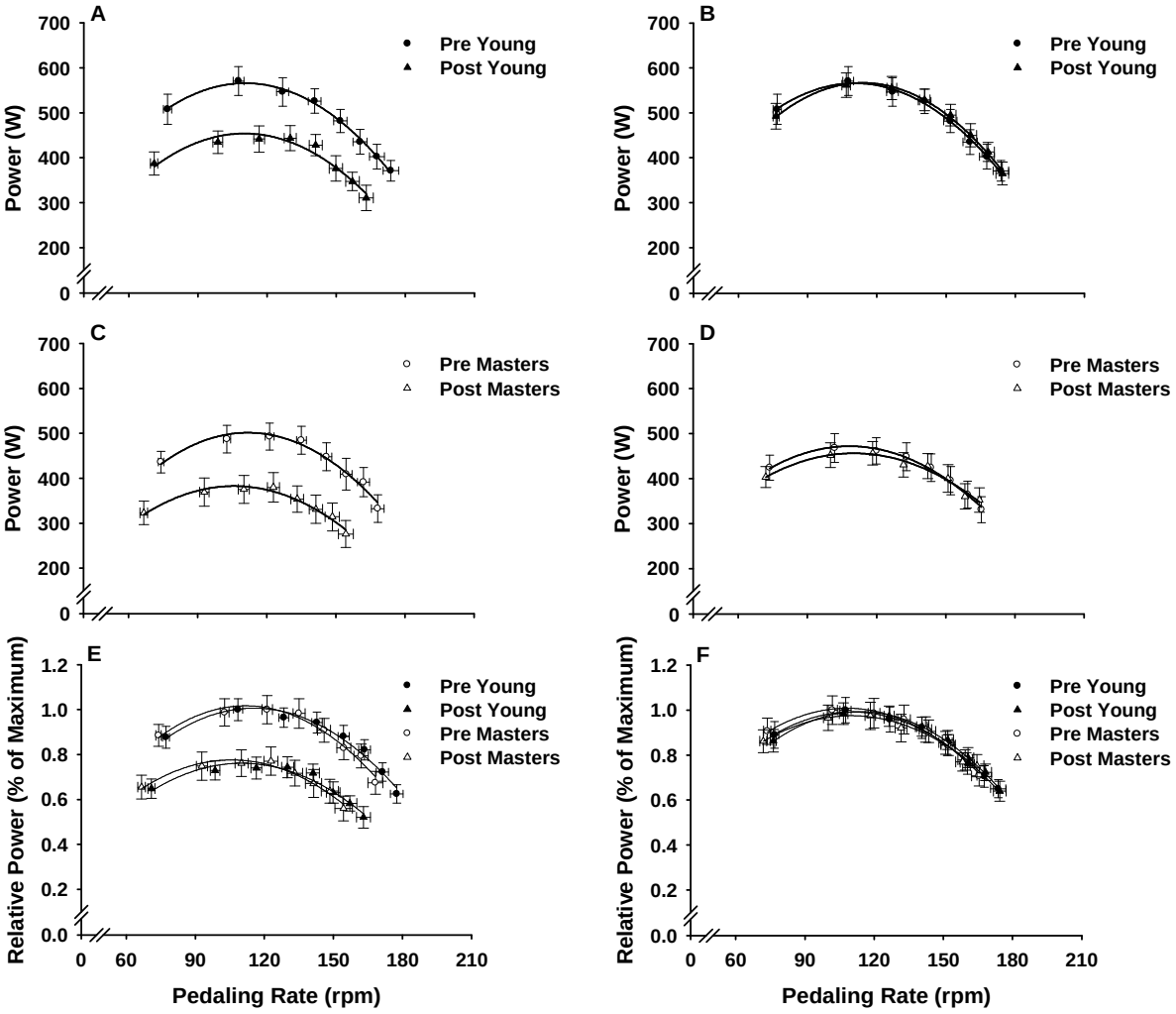

Figure 4.3: Power-pedaling rate relationships. Absolute (A, B, C, D) and relative (E, F) power-pedaling rate relationships for the fatigued ipsilateral (left panels) and rested contralateral (right panels) legs. Power-pedaling rate relationships for young and masters cyclists were shifted downward at 30 s post-TT for the fatigued ipsilateral leg, but did not change for the rested contralateral leg. Data are presented as mean ± SEM and are fitted with a quadratic equation.

5. SUMMARY, CONCLUSION, AND RECOMMENDATIONS

Summary

In this series of studies, I used high-intensity cycling exercise (i.e., 10 min TT) to induce fatigue and quantified fatigue via pre-to post-TT changes in maximum cycling power. The main finding of the first study was that exercise-induced changes in maximum cycling power manifested with differential power loss at each joint with ankle plantar flexion and knee flexion exhibiting relatively greater fatigue than knee extension and hip extension. However, changes in maximal joint-specific powers were not presaged by changes in submaximal joint-specific powers. These results suggest that exercise-induced fatigue can have distinct consequences for submaximal and maximal joint-specific power production. The novel finding in the second study was that maximum cycling power in the rested contralateral leg was maintained despite considerable power loss in the fatigued ipsilateral leg. This suggests that a cross-over of fatigue was not sufficient to measurably compromise maximum power of the rested contralateral leg when fatigue was induced via high-intensity endurance exercise involving a substantial muscle mass. In the third study, results indicated that power loss and recovery were nearly identical for young and masters cyclists despite a > 30 yr age difference. These results indirectly suggest that chronic endurance training may be beneficial for maintaining neuromuscular performance with advanced age. Collectively,

these findings extend upon previous results obtained from small muscle mass models and highlight functional changes associated with exercise-induced fatigue.

Conclusion

High-intensity cycling exercise substantially impaired maximum cycling power production. Further, reductions in maximum cycling power manifested with differential joint-specific power-loss across the ankle, knee, and hip. Exercise-induced impairments in maximal voluntary neuromuscular function were limited to only those muscles involved in the fatiguing task. Finally, fatigue induced via high intensity cycling has similar functional consequences for endurance trained young and masters cyclists.

Future Recommendations

Limitations to these investigations should be considered when interpreting these results but at the same time provide recommendations for future research. A limitation in the first study was the use of inverse dynamic techniques to quantify joint-specific powers and describe the biomechanics of producing muscular power during cycling. Although these methods are widely used (18, 35, 40), they cannot quantify individual muscle forces and activation patterns (90). A next step would be to use forward dynamic simulations to quantify individual muscle forces and activation patterns (90) in order to elucidate the contributions of neuromuscular fatigue and motor control to multijoint fatigue. A limitation associated with the single-leg cycling model is that the development of central fatigue and peripheral fatigue were not directly measured. Specifically, central fatigue is usually evaluated during a maximal isometric contraction of the exercising muscle. Similarly, exercise-induced peripheral muscle fatigue is usually quantified via

the reduction in force output in response to direct electric / magnetic motor nerve stimulation shortly after, or during, muscle contractions. I recommend that future investigators combine these two approaches in order to connect the underlying mechanisms of fatigue with the resulting functional outcomes. It is important to note that in these investigations, maximum cycling power may have partially recovered prior to the post-TT maximal cycling trial. The occurrence of such quick recovery is unlikely given that previous authors have reported that central (17, 34, 79) and peripheral fatigue (7-10, 12, 17, 34, 79) can last for several minutes. A methodological recommendation would be to have participants perform several maximal cycling trials at various time points during the TT to quantify the development of fatigue. Finally, it may be important to consider the effect of exercise-induced fatigue on changes in submaximal neuromuscular function as many voluntary movements require submaximal force and power production for prolonged periods of time.

REFERENCES

1. Abbiss CR, Karagounis LG, Laursen PB, Peiffer JJ, Martin DT, Hawley JA, Fatehee NN, Martin JC. Single-leg cycle training is superior to double-leg cycling in improving the oxidative potential and metabolic profile of trained skeletal muscle. *J Appl Physiol*. 2011;110(5):1248-55.

2. Abbiss CR, Quod MJ, Levin G, Martin DT, Laursen PB. Accuracy of the Velotron ergometer and SRM power meter. *Int J Sports Med*. 2009;30(2):107-12.

3. Allen D, Westerblad H. What limits exercise during high-intensity aerobic exercise? *Eur J Appl Physiol*. 2010;110(3):661-2; author reply 3-4.

4. Allen DG, Lamb GD, Westerblad H. Skeletal muscle fatigue: cellular mechanisms. *Physiol Rev*. 2008;88(1):287-332.

5. Allman BL, Rice CL. Incomplete recovery of voluntary isometric force after fatigue is not affected by old age. *Muscle Nerve*. 2001;24(9):1156-67.

6. Amann M. Central and peripheral fatigue: interaction during cycling exercise in humans. *Med Sci Sports Exerc*. In press.

7. Amann M, Dempsey JA. Locomotor muscle fatigue modifies central motor drive in healthy humans and imposes a limitation to exercise performance. *J Physiol*. 2008;586(1):161-73.

8. Amann M, Eldridge MW, Lovering AT, Stickland MK, Pegelow DF, Dempsey JA. Arterial oxygenation influences central motor output and exercise performance via effects on peripheral locomotor muscle fatigue in humans. *J Physiol*. 2006;575(Pt 3):937-52.

9. Amann M, Pegelow DF, Jacques AJ, Dempsey JA. Inspiratory muscle work in acute hypoxia influences locomotor muscle fatigue and exercise performance of healthy humans. *Am J Physiol Regul Integr Comp Physiol*. 2007;293(5):R2036-45.

10. Amann M, Proctor LT, Sebranek JJ, Pegelow DF, Dempsey JA. Opioid-mediated muscle afferents inhibit central motor drive and limit peripheral muscle fatigue development in humans. *J Physiol*. 2009;587(Pt 1):271-83.

11. Amann M, Romer LM, Pegelow DF, Jacques AJ, Hess CJ, Dempsey JA. Effects of arterial oxygen content on peripheral locomotor muscle fatigue. *J Appl Physiol*. 2006;101(1):119-27.

12. Amann M, Romer LM, Subudhi AW, Pegelow DF, Dempsey JA. Severity of arterial hypoxaemia affects the relative contributions of peripheral muscle fatigue to exercise performance in healthy humans. *J Physiol*. 2007;581(Pt 1):389-403.

13. Amann M, Subudhi A, Foster C. Influence of testing protocol on ventilatory thresholds and cycling performance. *Med Sci Sports Exerc*. 2004;36(4):613-22.

14. Bassey EJ, Fiatarone MA, O'Neill EF, Kelly M, Evans WJ, Lipsitz LA. Leg extensor power and functional performance in very old men and women. *Clin Sci (Lond)*. 1992;82(3):321-7.

15. Baudry S, Klass M, Pasquet B, Duchateau J. Age-related fatigability of the ankle dorsiflexor muscles during concentric and eccentric contractions. *Eur J Appl Physiol*. 2007;100(5):515-25.

16. Beelen A, Sargeant AJ. Effect of fatigue on maximal power output at different contraction velocities in humans. *J Appl Physiol*. 1991;71(6):2332-7.

17. Bentley DJ, Smith PA, Davie AJ, Zhou S. Muscle activation of the knee extensors following high intensity endurance exercise in cyclists. *Eur J Appl Physiol*. 2000;81(4):297-302.

18. Bezodis IN, Kerwin DG, Salo AI. Lower-limb mechanics during the support phase of maximum-velocity sprint running. *Med Sci Sports Exerc*. 2008;40(4):707-15.

19. Bigland-Ritchie B, Johansson R, Lippold OC, Woods JJ. Contractile speed and EMG changes during fatigue of sustained maximal voluntary contractions. *J Neurophysiol*. 1983;50(1):313-24.

20. Bilodeau M, Erb MD, Nichols JM, Joiner KL, Weeks JB. Fatigue of elbow flexor muscles in younger and older adults. *Muscle Nerve*. 2001;24(1):98-106.

21. Bini RR, Diefenthaeler F, Mota CB. Fatigue effects on the coordinative pattern during cycling: kinetics and kinematics evaluation. *J Electromyogr Kinesiol*. 2010;20(1):102-7.

22. Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med*. 1970;2(2):92-8.

23. Broker JP, Gregor RJ. Mechanical energy management in cycling: source relations and energy expenditure. *Med Sci Sports Exerc*. 1994;26(1):64-74.

24. Bundle MW, Ernst CL, Bellizzi MJ, Wright S, Weyand PG. A metabolic basis for impaired muscle force production and neuromuscular compensation during sprint cycling. *Am J Physiol Regul Integr Comp Physiol*. 2006;291(5):R1457-64.

25. Burnley M. The limit to exercise tolerance in humans: validity compromised by failing to account for the power-velocity relationship. *Eur J Appl Physiol*. 2010;109(6):1225-6.

26. Buttelli O, Vandewalle H, Jouanin JC, Seck D, Monod H. Effects of aerobic exercise on the torque-velocity relationship in cycling. *Eur J Appl Physiol Occup Physiol*. 1997;75(6):499-503.

27. Callahan DM, Foulis SA, Kent-Braun JA. Age-related fatigue resistance in the knee extensor muscles is specific to contraction mode. *Muscle Nerve*. 2009;39(5):692-702.

28. Christie A, Snook EM, Kent-Braun JA. Systematic review and meta-analysis of skeletal muscle fatigue in old age. *Med Sci Sports Exerc*. 2011;43(4):568-77.

29. Coggan AR, Spina RJ, Rogers MA, King DS, Brown M, Nemeth PM, Holloszy JO. Histochemical and enzymatic characteristics of skeletal muscle in master athletes. *J Appl Physiol*. 1990;68(5):1896-901.

30. Dalton BH, Power GA, Vandervoort AA, Rice CL. Power loss is greater in old men than young men during fast plantar flexion contractions. *J Appl Physiol*. 2010;109:1441–7.

31. Dalton BH, Power GA, Vandervoort AA, Rice CL. Power loss is greater in old men than young men during fast plantar flexion contractions. *J Appl Physiol*. in press.

32. Davis JM, Bailey SP. Possible mechanisms of central nervous system fatigue during exercise. *Med Sci Sports Exerc*. 1997;29(1):45-57.

33. de Leva P. Adjustments to Zatsiorsky-Seluyanov's segment inertia parameters. *J Biomech*. 1996;29:1223-30.

34. Decorte N, Lafaix PA, Millet GY, Wuyam B, Verges S. Central and peripheral fatigue kinetics during exhaustive constant-load cycling. *Scand J Med Sci Sports*. In press.

35. DeVita P, Helseth J, Hortobagyi T. Muscles do more positive than negative work in human locomotion. *J Exp Biol*. 2007;210(Pt 19):3361-73.

36. Ditor DS, Hicks AL. The effect of age and gender on the relative fatigability of the human adductor pollicis muscle. *Can J Physiol Pharmacol*. 2000;78(10):781-90.

37. Elftman H. Forces and energy changes in the leg during walking. *Am J Physiol*. 1939;125:357-66.

38. Elmer SJ, Barrett P, Korff T, Martin JC. Joint-specific power production during submaximal and maximal cycling. *Med Sci Sports Exerc*. 2011;(Doi: 10.1249/MSS.0b013e31821b00c5).

39. Enoka RM, Stuart DG. Neurobiology of muscle fatigue. *J Appl Physiol*. 1992;72(5):1631-48.

40. Ericson MO. Mechanical muscular power output and work during ergometer cycling at different work loads and speeds. *Eur J Appl Physiol Occup Physiol*. 1988;57(4):382-7.

41. Fell J, Haseler L, Gaffney P, Reaburn P, Harrison G. Performance during consecutive days of laboratory time-trials in young and veteran cyclists. *J Sports Med Phys Fitness*. 2006;46(3):395-402.

42. Fernandez-Del-Olmo M, Rodriguez FA, Marquez G, Iglesias X, Marina M, Benitez A, Vallejo L, Acero RM. Isometric knee extensor fatigue following a Wingate test: peripheral and central mechanisms. *Scand J Med Sci Sports*. In press.

43. Fitts RH, Holloszy JO. Lactate and contractile force in frog muscle during development of fatigue and recovery. *Am J Physiol*. 1976;231(2):430-3.

44. Foldvari M, Clark M, Laviolette LC, Bernstein MA, Kaliton D, Castaneda C, Pu CT, Hausdorff JM, Fielding RA, Singh MA. Association of muscle power with functional status in community-dwelling elderly women. *J Gerontol A Biol Sci Med Sci*. 2000;55(4):M192-9.

45. Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. *Physiol Rev*. 2001;81(4):1725-89.

46. Gandevia SC, Allen GM, Butler JE, Taylor JL. Supraspinal factors in human muscle fatigue: evidence for suboptimal output from the motor cortex. *J Physiol*. 1996;490 (Pt 2):529-36.

47. Gardner AS, Stephens S, Martin DT, Lawton E, Lee H, Jenkins D. Accuracy of SRM and power tap power monitoring systems for bicycling. *Med Sci Sports Exerc*. 2004;36(7):1252-8.

48. Hautier CA, Linossier MT, Belli A, Lacour JR, Arsac LM. Optimal velocity for maximal power production in non-isokinetic cycling is related to muscle fibre type composition. *Eur J Appl Physiol Occup Physiol*. 1996;74(1-2):114-8.

49. Hicks AL, McCartney N. Gender differences in isometric contractile properties and fatigability in elderly human muscle. *Can J Appl Physiol*. 1996;21(6):441-54.

50. Kent-Braun JA, Callahan DM, Foulis SA, Chung LH. Muscle fatigue in elderly people. In: C Williams and S Ratel editors. *Human Muscle Fatigue*. New York: Routledge; 2009, pp. 103-34.

51. Klausen K, Secher NH, Clausen JP, Hartling O, Trap-Jensen J. Central and regional circulatory adaptations to one-leg training. *J Appl Physiol*. 1982;52(4):976-83.

52. Lanza IR, Russ DW, Kent-Braun JA. Age-related enhancement of fatigue resistance is evident in men during both isometric and dynamic tasks. *J Appl Physiol*. 2004;97(3):967-75.

53. Louis J, Hausswirth C, Bieuzen F, Brisswalter J. Muscle strength and metabolism in master athletes. *Int J Sports Med*. 2009;30(10):754-9.

54. MacIntosh BR, Fletcher JR. The parabolic power-velocity relationship does apply to fatigued states. *Eur J Appl Physiol*. 2011;111(2):319-20.

55. MacIntosh BR, Fletcher JR. Reply to: Reply to: The parabolic power-velocity relationship does apply to fatigued states. *Eur J Appl Physiol*. In press.

56. Marcora SM, Staiano W. The limit to exercise tolerance in humans: mind over muscle? *Eur J Appl Physiol*. 2010;109(4):763-70.

57. Marcora SM, Staiano W. The parabolic power-velocity relationship does not apply to fatigued states. *Eur J Appl Physiol*. 2010;109(4):787-8.

58. Marcora SM, Staiano W. Reply to: The parabolic power-velocity relationship does apply to fatigued states. *Eur J Appl Physiol*. 2011;111(4):731-2.

59. Martin JC, Brown NA. Joint-specific power production and fatigue during maximal cycling. *J Biomech*. 2009;42(4):474-9.

60. Martin JC, Milliken DL, Cobb JE, McFadden KL, Coggan AR. Validation of a Mathematical Model for Road Cycling Power. *J Appl Biomech*. 1998;14(3):276-91.

61. Martin JC, Wagner BM, Coyle EF. Inertial-load method determines maximal cycling power in a single exercise bout. *Med Sci Sports Exerc*. 1997;29(11):1505-12.

62. Martin PG, Rattey J. Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. *Pflugers Arch*. 2007;454(6):957-69.

63. McKenna MJ, Hargreaves M. Resolving fatigue mechanisms determining exercise performance: integrative physiology at its finest! *J Appl Physiol*. 2008;104(1):286-7.

64. McNeil CJ, Rice CL. Fatigability is increased with age during velocity-dependent contractions of the dorsiflexors. *J Gerontol A Biol Sci Med Sci*. 2007;62(6):624-9.

65. Merton PA. Voluntary strength and fatigue. *J Physiol*. 1954;123(3):553-64.

66. Millet GY, Martin V, Lattier G, Ballay Y. Mechanisms contributing to knee extensor strength loss after prolonged running exercise. *J Appl Physiol*. 2003;94(1):193-8.

67. Neptune RR, Hull ML. Accuracy assessment of methods for determining hip movement in seated cycling. *J Biomech*. 1995;28(4):423-37.

68. Petrella JK, Kim JS, Tuggle SC, Hall SR, Bamman MM. Age differences in knee extension power, contractile velocity, and fatigability. *J Appl Physiol*. 2005;98(1):211-20.

69. Place N, Lepers R, Deley G, Millet GY. Time course of neuromuscular alterations during a prolonged running exercise. *Med Sci Sports Exerc*. 2004;36(8):1347-56.

70. Power GA, Dalton BH, Behm DG, Vandervoort AA, Doherty TJ, Rice CL. Motor unit number estimates in masters runners: use it or lose it? *Med Sci Sports Exerc*. 2010;42(9):1644-50.

71. Quod MJ, Martin DT, Martin JC, Laursen PB. The power profile predicts road cycling MMP. *Int J Sports Med*. 2010;31(6):397-401.

72. Rattey J, Martin PG, Kay D, Cannon J, Marino FE. Contralateral muscle fatigue in human quadriceps muscle: evidence for a centrally mediated fatigue response and cross-over effect. *Pflugers Arch*. 2006;452(2):199-207.

73. Ross EZ, Goodall S, Stevens A, Harris I. Time course of neuromuscular changes during running in well-trained subjects. *Med Sci Sports Exerc*. 2010;42(6):1184-90.

74. Ross EZ, Middleton N, Shave R, George K, Nowicky A. Corticomotor excitability contributes to neuromuscular fatigue following marathon running in man. *Exp Physiol*. 2007;92(2):417-26.

75. Sanderson DJ, Black A. The effect of prolonged cycling on pedal forces. *J Sports Sci*. 2003;21(3):191-9.

76. Sargeant AJ. Effect of muscle temperature on leg extension force and short-term power output in humans. *Eur J Appl Physiol Occup Physiol*. 1987;56(6):693-8.

77. Sargeant AJ, Dolan P. Effect of prior exercise on maximal short-term power output in humans. *J Appl Physiol*. 1987;63(4):1475-80.

78. Seck D, Vandewalle H, Decrops N, Monod H. Maximal power and torque-velocity relationship on a cycle ergometer during the acceleration phase of a single all-out exercise. *Eur J Appl Physiol Occup Physiol*. 1995;70(2):161-8.

79. Sidhu SK, Bentley DJ, Carroll TJ. Locomotor exercise induces long-lasting impairments in the capacity of the human motor cortex to voluntarily activate knee extensor muscles. *J Appl Physiol*. 2009;106(2):556-65.

80. Stackhouse SK, Stevens JE, Lee SC, Pearce KM, Snyder-Mackler L, Binder-Macleod SA. Maximum voluntary activation in nonfatigued and fatigued muscle of young and elderly individuals. *Phys Ther*. 2001;81(5):1102-9.

81. Steiner JL, Murphy EA, McClellan JL, Carmichael MD, Davis JM. Exercise Training Increases Mitochondrial Biogenesis in the Brain. *J Appl Physiol*. 2011;111:1066-71.

82. Tanaka H, Seals DR. Invited Review: Dynamic exercise performance in Masters athletes: insight into the effects of primary human aging on physiological functional capacity. *J Appl Physiol*. 2003;95(5):2152-62.

83. Tanaka H, Seals DR. Endurance exercise performance in Masters athletes: age-associated changes and underlying physiological mechanisms. *J Physiol*. 2008;586(1):55-63.

84. Taylor JL, Gandevia SC. A comparison of central aspects of fatigue in submaximal and maximal voluntary contractions. *J Appl Physiol*. 2008;104(2):542-50.

85. Todd G, Petersen NT, Taylor JL, Gandevia SC. The effect of a contralateral contraction on maximal voluntary activation and central fatigue in elbow flexor muscles. *Exp Brain Res*. 2003;150(3):308-13.

86. van Ingen Schenau GJ, van Woensel WW, Boots PJ, Snackers RW, de Groot G. Determination and interpretation of mechanical power in human movement: application to ergometer cycling. *Eur J Appl Physiol Occup Physiol*. 1990;61(1-2):11-9.

87. Vandervoort AA. Aging of the human neuromuscular system. *Muscle Nerve*. 2002;25(1):17-25.

88. Woltring HJ. A FORTRAN package for generalized, cross validatory spline smoothing and differentiation. *Adv Eng Software*. 1986;8:104-13.

89. Yano T, Yunoki T, Ogata H. Relationship between the slow component of oxygen uptake and the potential reduction in maximal power output during constant-load exercise. *J Sports Med Phys Fitness*. 2001;41(2):165-9.

90. Zajac FE, Neptune RR, Kautz SA. Biomechanics and muscle coordination of human walking. Part I: introduction to concepts, power transfer, dynamics and simulations. *Gait Posture*. 2002;16(3):215-32.